MUCOSAL HEALING IN ULCERATIVE COLITIS: A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY

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DEDICATED TO

MY WIFE, SON AND PARENTS

I would like to express my deepest gratitude to my family, who have been my rock throughout this journey. To my wife, Dr Ifrah Jahan, your love and support gave me the strength to pursue my dreams despite the distance. I am forever grateful for your sacrifices and encouragement.

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ABBREVIATIONS

5 ASA	5 Amino salicylic acid
ACT 1	Active ulcerative colitis 1 trial
ACT 2	Active ulcerative colitis 2 trial
BLI	Blue light imaging
BLI-BRT	Blue light imaging bright
BMI	Body mass index
FC	Fecal calprotectin
FMT	Fecal microbiota transplant
GS	Geboes score
HEMI	Histologic endoscopic mucosal improvement
HEMR	Histologic endoscopic mucosal remission
IBD	Inflammatory bowel disease
LCI	Linked color imaging
MES	Mayo endoscopic score
MH	Mucosal healing
MUAC	Mid upper arm circumference

NHI	Nancy histological index
PMS	Partial mayo score
SCCAI	Simple clinical colitis activity index
TNF	Tumor necrosis factor
Tofa	Tofacitinib
UC	Ulcerative colitis
UCEIS	Ulcerative colitis endoscopic index of severity
WLE	White light endoscopy
WLI	White light imaging

ABSTRACT

Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by relapsing-remitting mucosal inflammation. Accurate assessment of mucosal healing (MH) is crucial for optimal management and improved long-term outcomes. Traditional white light endoscopy (WLE) has limitations in detecting subtle mucosal changes, while linked color imaging (LCI) offers enhanced visualization.

Aims and Objectives: This study aims to evaluate endoscopic and histological disease activity in UC patients in symptomatic remission and to assess the correlation between WLE, LCI, and histology.

Materials & Methods: This prospective study included 103 ulcerative colitis patients in symptomatic remission. Endoscopic evaluations were performed using both WLE and LCI, with mucosal healing assessed by the mayo endoscopic sub-score (MES). LCI images were classified into three subgroups (A: no redness, B: redness with visible vessels, C: redness with obliterated vessels). Histological inflammation was evaluated using the Nancy Histology Index (NHI) from biopsy samples, and the LCI index was calculated using the CIELAB color space. Correlations between WLE, LCI, and histology were assessed. ROC curves and Kappa agreement were used to compare the accuracy of both techniques in predicting histological remission.

Results: The study patients predominantly aged 31-40 years, with 62.1% female and 68.9% presenting with left-sided colitis. While 88.4% were in endoscopic remission (MES 0 or 1), only 49.5% had histological remission (NHI 0). LCI showed significantly higher correlation than WLE with histological disease activity (Spearman's rho = 0.737 vs. 0.449, $p<0.001$). LCI index values increased with histological severity, and LCI outperformed WLE in predicting histological remission (AUROC 0.815 vs. 0.678 p-value <0.001). LCI A showed stronger agreement with NHI 0 than MES 0 (kappa = 0.539 vs. 0.322, z-score = 2.23, $p<0.05$), making LCI a more reliable predictor of histological remission.

Conclusion: LCI is a more accurate and objective tool for assessing mucosal healing in UC patients compared to WLE. With stronger correlations to histological outcomes, LCI has the potential to improve clinical decision-making, reduce biopsy needs, and better predict long-term outcomes. Future studies should focus on validating these findings in larger cohorts and defining standardized LCI index threshold for clinical use.

KEYWORDS: Ulcerative Colitis, mucosal healing, white light endoscopy, LCI.

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INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that primarily affects the colon, causing continuous superficial mucosal inflammation extending from the rectum to varying extents of the colon, and is characterized by a relapsing-remitting course.[1] The typical clinical manifestations of UC include bloody diarrhea, with or without mucus, rectal urgency, tenesmus, and varying degrees of abdominal pain, often relieved by defecation. Some patients, though in the minority, may experience constipation.[2] UC is diagnosed through a combination of clinical features, endoscopic observations, histological evidence, and the exclusion of other potential diagnoses. The definitive diagnosis is made by colonoscopy with biopsy.[3] A hallmark finding of UC is continuous colonic inflammation, which is characterized by erythema, loss of the normal vascular pattern, granularity, erosions, friability, bleeding, and ulcerations, with a clear demarcation between inflamed and non-inflamed bowel.[4] Histological characteristics of UC include crypt architecture distortion, crypt shortening, crypt abscesses, cellular infiltrates with plasma cells (basal plasmacytosis), increased lymphocytes in the lamina propria, mucin depletion, and paneth cell metaplasia.[5] Approximately 40% of patients present with proctitis at the time of diagnosis, 30% with left-sided colitis, and 30% with pancolitis. The disease progression tends to be gradual, with only 14%–16% of patients progressing from proctitis to pancolitis. Over a 10-year period, about 50%–55% of patients will experience remission, 37% will follow a chronic, intermittent course, 6% will develop a chronic continuous course, and 1% will experience low activity followed by a significant flare-up. Roughly 20%–30% of patients require colectomy after 25 years of disease activity. Despite this, overall mortality in UC patients is similar to that of matched controls, though those with new or extensive disease have increased mortality risks.[6]

The treatment approach for UC is guided by factors such as disease severity, distribution, age of onset, disease duration, disease course, relapse frequency, previous medication use, medication side effects,

and extra-intestinal manifestations. Remission is generally defined by the cessation of rectal bleeding, improved bowel habits, and endoscopic healing, as indicated by a mayo score of zero or one, although clinical symptoms do not always correspond to endoscopic findings.[7] Some patients in clinical remission may still have active colonic inflammation.[8] Achieving endoscopic healing is critical, as it is associated with improved long-term remission, reduced need for colectomy, and less reliance on corticosteroids.[9] Liverani et al. proposed an algorithm for predicting clinical relapse based on clinical and biological markers, suggesting that those at higher risk for relapse tend to have an early age of onset, extensive disease, multiple prior relapses, and fecal calprotectin levels greater than 190 µg/g on repeated testing.[10] On average, 70%–80% of patients have a cumulative relapse risk within 10 years, and nearly 50% require UC-related hospitalization. Additionally, the 10-year cumulative colectomy risk is around 10%–15%.[11] The treat-to-target (T2T) approach, which advocates for treatment strategies based on specific therapeutic targets, has gained prominence in IBD treatment, aiming to improve long-term outcomes.

Mucosal healing (MH) has become a recognized therapeutic goal in UC management.[12] Increasing evidence suggests that MH is associated with improved clinical outcomes, including sustained remission, reduced hospitalization rates, decreased surgical interventions, and a lower risk of colorectal cancer.[13] Despite its importance, there is no universally accepted definition of MH, and criteria for assessing disease activity vary. Endoscopic indices such as the Mayo Endoscopic sub score (MES) and the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) have been developed to standardize the assessment of MH.[14-15] In both clinical trials and practice, a MES of 0 or 1 is widely accepted as a criterion for MH.[16] However, these scoring systems are subjective, leading to variability in endoscopic assessments between observers. Meta-analysis have shown that an MES of 1 is associated with increased risk of relapse as compared to an MES of 0.[17] Even quiescent UC patients with an MES

of 0 have a relapse rate of about 10% within the first 6 months of follow-up.[18] The STRIDE-II program recommends a MES of 0 or a UCEIS ≤1 as targets for endoscopic healing in UC treatment, and it also suggests histological healing as an important goal.[19] Persistent microscopic inflammation, even in endoscopically quiescent disease, is linked to higher relapse rates.[20] Histological healing has garnered more attention as a target beyond endoscopic remission, as studies indicate that histological indices can assess colonic inflammation more accurately than endoscopic indices, even in patients with mild clinical symptoms.[21-22]Additionally, histological factors have been shown to predict clinical relapse and long-term outcomes in quiescent UC patients.[23] Discrepancies between endoscopic and histological findings further emphasize the need for accurate disease assessment.[24] Thus, evaluating intestinal inflammation accurately is vital for optimizing UC management and sustaining remission.[25]

Endoscopic technologies continue to evolve, offering new methods for assessing intestinal inflammation. Techniques such as magnifying chromoendoscopy, narrow-band imaging, confocal endoscopy, and endocytoscopy are now available for detailed histological inflammation evaluation and mucosal healing detection.[26-29] These advanced modalities not only help detect intestinal inflammation but are also instrumental in identifying UC-associated neoplasia.[30-31] Fujifilm has introduced an endoscopic system called “LASEREO,” which employs two lasers as the light source instead of the conventional Xenon lamp. One laser provides white light by exciting a phosphor at the endoscope tip, while the other offers short-wavelength light for Blue Light Imaging (BLI). The BLI light is a combination of a strong 410 nm laser, a weaker 450 nm laser, and fluorescent light. The LASEREO system offers three observation modes: BLI, BLI-bright (BLI-BRT), and white light. The BLI-BRT mode is brighter and designed to enhance gastrointestinal neoplastic lesion detection. The system also includes linked color imaging (LCI), a feature that enhances mucosal color differentiation, making reddish areas appear redder and white areas whiter, which improves the detection and recognition of neoplasms.[32-33] LCI has

demonstrated utility in inflammation evaluation, including helicobacter pylori detection and the identification of subtle changes in reflux esophagitis.[34-35] LCI has also proven effective in detecting early gastric cancer and colorectal tumors.[36-37] Few studies have explored LCI usefulness for assessing intestinal inflammation in IBD patients.[38]

If mucosal inflammation in UC patients could be assessed using LCI without tissue biopsy, it would significantly reduce diagnostic invasiveness and costs. Conventional white light endoscopy has limitations in predicting histological inflammation and relapse risk, even when endoscopic findings suggest remission. This study aims to evaluate the correlation between mucosal healing, as assessed by white light imaging (WLI), linked color imaging (LCI), and histological activity in UC patients. The goal is to enhance the comprehensive evaluation of disease activity and progression, ultimately improving UC patient management and outcomes.

AIMS AND OBJECTIVES

- To evaluate the endoscopic and histological disease activity in ulcerative colitis patients in symptomatic remission.
- To evaluate the correlation between white light endoscopy, linked color imaging and histology in patients with ulcerative colitis in symptomatic remission.

REVIEW OF LITERATURE

Over time, treatment goals for UC have evolved from symptomatic management to achieving more comprehensive outcome like deep remission, including mucosal healing (MH). Mucosal healing is increasingly recognized as a key target in managing UC, as achieving it is linked to better long-term outcomes such as sustained remission, reduced hospitalization, and decreased risk of surgery.[12,39-42]

The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative, developed by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD), was first introduced in 2015 to propose treatment targets for inflammatory bowel disease (IBD). These targets aimed to improve long-term outcomes by incorporating clinical remission and endoscopic healing as essential goals. However, with advances in IBD management, it became necessary to update the original STRIDE framework, leading to the development of STRIDE-II, which incorporates additional treatment targets for both adult and pediatric IBD patients. STRIDE-II represents an extensive effort by the IOIBD to refine and expand the treatment targets for IBD. Based on a systematic review of the literature and consensus from 89 IOIBD members, the initiative reviewed over 11,000 manuscripts and ultimately incorporated 435 studies into their analysis. Through multiple rounds of surveys and voting, consensus was reached on 13 out of 15 proposed recommendations. These recommendations were endorsed when at least 75% of participants rated the recommendation highly on a 10-point scale. STRIDE-II confirmed the original STRIDE-I long-term targets of clinical remission and endoscopic healing, reinforcing their importance in disease management. Additionally, STRIDE-II introduced new long-term targets, including the absence of disability, the restoration of quality of life, and normal growth in children, reflecting the broader concerns of both adult and pediatric patients with IBD. In terms of short-term targets, symptomatic relief and the normalization of serum and fecal markers (such as C-reactive protein [CRP], erythrocyte sedimentation

rate [ESR], and calprotectin) were highlighted as key objectives. These markers serve as indicators of inflammation and help in the early detection of disease activity. Monitoring these biomarkers regularly allows for better disease control and timely therapeutic adjustments. Although transmural healing in crohn's disease and histologic healing in ulcerative colitis were not formally endorsed as therapeutic targets in STRIDE-II, they are still considered important indicators of the depth of remission. STRIDE-II emphasizes the value of achieving deeper levels of healing, as histological healing has been shown to predict sustained remission and improved long-term outcomes, especially in UC patients (Turner et al). One of the key messages of STRIDE-II is that the treat-to-target (T2T) approach must be adapted to the individual patient, taking into account their disease characteristics, co-morbidities and local resources. While endoscopic healing remains a universal goal, the pathway to achieving these targets can vary between patients. This personalized approach ensures that treatments are tailored to the specific needs of each patient, which may include the use of biologics or other therapies aimed at achieving both symptom relief and deep remission.[19]

Mucosal healing (MH) has gained increasing recognition as an important therapeutic target in the management of ulcerative colitis.[43-44] In the study conducted by P. B. Carvalho et al., they aimed to assess the differences in clinical relapse rates over a 12-month period between UC patients with MES of 0 and 1. The research involved a retrospective cohort of consecutive UC patients who were in corticosteroid-free remission between 2008 and 2013, with a minimum follow-up period of one year. Patients included in the study were classified based on their MES scores, obtained through complete colonoscopy, into two groups: MES 0 (complete mucosal healing) and MES 1 (minimal residual inflammation). The study revealed that clinical relapse was significantly more frequent in patients with MES 1 than in those with MES 0. Specifically, 27.3% of patients with MES 1 experienced a relapse during the follow-up period, compared to only 11.5% of those with MES 0 ($p = 0.022$). In multivariate analysis, MES 1

emerged as the only factor significantly associated with an increased risk of relapse, with an odds ratio of 2.89 (95% confidence interval 1.14–7.36, p = 0.026). This association was particularly evident in patients with left-sided or extensive colitis, where those with MES 1 had a threefold higher risk of relapse compared to those with MES 0. The findings of this study support the notion that achieving a MES of 0, indicating complete mucosal healing, should be considered the optimal treatment endpoint for UC. The data demonstrated that even minor residual inflammation, as reflected by an MES of 1, is associated with a significantly higher risk of disease relapse. This reinforces the clinical utility of endoscopic scoring systems in guiding therapeutic decisions and underscores the need for more stringent treatment goals aimed at achieving complete mucosal healing.[45]

Infliximab, a biologic therapy targeting tumor necrosis factor (TNF), has demonstrated efficacy in inducing clinical remission and MH in patients with moderate to severe ulcerative colitis. The Active Ulcerative Colitis Trials (ACT-1 and ACT-2) highlighted the superiority of infliximab over placebo in achieving these outcomes.[46] A follow-up study conducted by Colombel et al. examined the association between early mucosal healing (as measured by endoscopic scores) and long-term clinical outcomes, including colectomy rates, symptom improvement, and corticosteroid use. Patients from the ACT-1 and ACT-2 trials underwent endoscopic evaluations at baseline, week 8, week 30, and week 54 (in ACT-1). Mucosal healing was defined as a MES of 0 (normal) or 1 (mild). By week 8, patients were categorized into four subgroups based on their MES 0–3, and the study aimed to determine whether early mucosal healing at week 8 predicted long-term clinical outcomes, including the need for colectomy and corticosteroid use, at weeks 30 and 54. Patients treated with infliximab who achieved lower endoscopic scores at week 8 were significantly less likely to undergo colectomy during the 54-week follow-up (P = 0.0004). This association between mucosal healing and reduced colectomy risk was not observed in the placebo group (P = 0.47). Additionally, patients with better endoscopic outcomes at week 8 also experienced superior symptom control and

reduced corticosteroid use at weeks 30 and 54 (P = 0.0001 in the infliximab group; P = 0.01 in the placebo group). Among patients who demonstrated a clinical response by week 8, a similar trend was observed, wherein lower MES were associated with better long-term outcomes. However, for those who achieved full clinical remission at week 8, the degree of mucosal healing did not appear to significantly predict the subsequent course of the disease. This study underscores the importance of achieving early mucosal healing with infliximab in UC patients. The degree of mucosal healing at week 8 was closely linked with improved long-term outcomes, including a reduced risk of colectomy and better overall symptom management. These findings suggest that achieving mucosal healing early in the treatment course should be a key therapeutic goal, as it not only leads to immediate symptom relief but also predicts favorable long-term clinical outcomes.[39]

Recent systematic reviews and meta-analyses have provided insights into the significance of MH in predicting long-term outcomes for UC patients. Shah et al. (2024) conducted a comprehensive systematic review and meta-analysis to evaluate whether achieving mucosal healing at the first endoscopic evaluation after initiating UC therapy correlates with improved long-term outcomes. Their study analyzed data from 13 studies involving 2,073 patients with active UC. The primary aim was to assess clinical remission after at least 52 weeks, with secondary outcomes including rates of colectomy, corticosteroid use, and long-term MH. The analysis revealed that patients who achieved MH at the initial endoscopic evaluation had significantly higher odds of long-term clinical remission (odds ratio [OR] 4.50; 95% confidence interval [CI], 2.12–9.52) compared to those who did not achieve MH. Additionally, these patients had higher odds of remaining free of colectomy (OR 4.15; 95% CI, 2.53–6.81) and achieving long-term MH (OR 8.40; 95% CI, 3.13–22.53). Notably, there was no significant difference in outcomes based on whether patients received biologic or non-biologic therapy. These findings underscore the importance of achieving MH as a treatment goal in UC, highlighting its

association with favorable long-term outcomes, including clinical remission, avoidance of colectomy, and corticosteroid-free remission. The evidence supports the integration of MH into therapeutic strategies for UC, aligning with the evolving standards of care. In conclusion, the systematic review by Shah et al. provides robust evidence that mucosal healing is a valuable endpoint in UC management, offering substantial benefits in terms of long-term disease control and reduced need for surgical intervention.[9]

MH has emerged as the primary therapeutic target in the treatment of UC due to its association with reduced risk of disease reactivation and improved long-term outcomes.[19,47] However, evidence suggests that histologic activity may persist in patients with apparent MH, and this lingering histologic inflammation may account for relapses in some patients despite endoscopic healing. A study by Laterza et al. (2024) aimed to assess the presence of histologic activity in UC patients with mucosal healing, as indicated by a MES of 0 or 1, and to identify which histologic lesions were predictive of disease relapse. In this retrospective study, 100 UC patients who demonstrated MH on colonoscopy were enrolled. Histologic reports of biopsies were reviewed to evaluate typical UC lesions, and clinical outcomes were followed for 12 months to document relapses. The study found that histologic lesions were present in the vast majority of patients despite achieving MH. Only two patients showed no histological signs of inflammation. Univariate analysis revealed that patients with a higher number of baseline histologic lesions had an increased risk of relapse (OR 1.25, $p = 0.012$). Specific histological features such as basal plasmacytosis (OR 4.33, $p = 0.005$), lamina propria eosinophils (OR 2.99, $p = 0.047$), and surface irregularity (OR 4.70, $p = 0.010$) were all significantly associated with a higher likelihood of disease reactivation. Furthermore, multivariate analysis confirmed basal plasmacytosis (OR 2.98, $p = 0.050$) and surface irregularity (OR 4.50, $p = 0.024$) as independent risk factors for relapse in UC patients with MH. These findings suggest that despite achieving MH, histologic disease may persist and contribute to future relapses. As such, histologic healing

should be considered a crucial endpoint in UC management, as achieving MH alone may not fully prevent disease reactivation.[48]

Histologic healing is increasingly recognized as a crucial therapeutic target in UC as many studies have found that persistent histologic activity is associated with higher relapse rates.[49-56] While clinical and endoscopic remission have been widely studied, histologic healing—indicative of deeper remission—has not been extensively evaluated, particularly in patients undergoing conventional treatment. The prospective cohort study by Ø Steinsbø, A Carlsen et al. investigates the rates of deep and complete remission following 3 months of conventional treatment in newly diagnosed UC patients with moderate to severe endoscopic activity. The study aimed to assess the rates of deep remission (clinical remission plus mucosal healing) and complete remission (deep remission plus histologic healing) in UC patients after initiating conventional therapies, including 5-aminosalicylate, corticosteroids, and azathioprine. Additionally, the study explored baseline clinical and biochemical variables that could predict complete remission after treatment. A total of 180 patients were included, with clinical, biochemical, endoscopic, and histologic data collected at both baseline and after 3 months. The study reported that 62.8% of patients achieved deep remission, while 42.2% achieved complete remission. Notably, one-third of patients who exhibited mucosal healing (Mayo Endoscopic Score ≤ 1) still had histologic activity (Nancy Index ≥ 1). These findings underscore the discordance between endoscopic and histologic healing, emphasizing the importance of targeting histologic healing to achieve complete remission. The study identified several baseline predictors of complete remission. Patients with less extensive disease involvement and moderate endoscopic activity were more likely to achieve complete remission. Specifically, patients with limited disease distribution and moderate inflammation at baseline had a higher likelihood of achieving complete remission, with an odds ratio of 4.1 (95% CI: 7.69–2.18). In contrast, patients with pan-colitis and severe inflammatory activity at baseline were less likely to achieve complete remission. The findings of this study are clinically significant,

as they highlight the high prevalence of histologic activity even in patients who achieve mucosal healing. Persistent histologic inflammation was associated with higher symptom scores and elevated fecal calprotectin levels, indicating that targeting histologic healing may reduce disease activity and improve long-term outcomes in UC patients. This study supports the need for more stringent treatment goals aimed at achieving both endoscopic and histologic remission in UC management.[57]

Recent studies have highlighted the importance of MH in managing UC, particularly focusing on histologic endoscopic mucosal improvement (HEMI) and histologic endoscopic mucosal remission (HEMR) as treatment targets. A pivotal study by Parkes et al. (2023) investigated the clinical relevance of achieving these endpoints in the context of a phase 3 maintenance trial of upadacitinib, a medication for moderately to severely active UC. The study assessed clinical and patient-reported outcomes in patients who had a clinical response following 8- or 16-week upadacitinib induction therapy and then received 52 weeks of maintenance treatment. The researchers conducted both cross-sectional and predictive analyses to explore the relationship between achieving HEMR or HEMI at Week 8, week 16 and the subsequent outcomes at Week 52.Cross-sectional analyses indicated that patients achieving HEMR had significantly greater odds of achieving favorable clinical and patient-reported outcomes at week 52 compared to those who did not achieve HEMI. Specifically, predictive analyses demonstrated that patients with HEMR at Week 8 and week 16 had notably higher odds of reaching clinical remission (adjusted odds ratio [aOR] = 3.6; $p = 0.001$) and endoscopic remission (aOR = 3.9; $p < 0.001$) at week 52 compared to those not achieving HEMI and HEMR. For those achieving HEMI without HEMR, the odds were somewhat lower: clinical remission (aOR = 3.2; $p < 0.001$) and endoscopic remission (aOR = 2.4; $p = 0.010$). Furthermore, the study found that patients achieving HEMR had no hospitalizations or surgeries at Week 52, underscoring the clinical significance of this more stringent endpoint. Although patient-reported outcomes showed

similar trends for both HEMI and HEMR, statistical differences were not observed between these groups. In summary, Parkes et al. (2023) demonstrate that while both HEMI and HEMR are clinically relevant, achieving HEMR is associated with a higher likelihood of improved long-term clinical and patient-reported outcomes. This reinforces the role of stringent mucosal healing targets in optimizing UC management and improving patient outcomes.[58]

The use of biological therapies such as infliximab, adalimumab, golimumab, and vedolizumab has transformed the treatment of UC.[59-67] However, only a small proportion of patients achieve clinical remission, and an even lower percentage attain MH, the key therapeutic target in UC management. Fecal calprotectin (FC), a non-invasive biomarker of intestinal inflammation, has shown promise as an early predictor of therapeutic response, particularly in the context of MH.[68-78] The prospective study by Bertani et al. aimed to evaluate the role of FC as a predictive marker for mucosal healing in UC patients receiving biological therapy. This study enrolled 109 UC patients who initiated biological therapy at the study center. Biological agents included infliximab, adalimumab, golimumab, and vedolizumab. Patients underwent colonoscopy at baseline and at week 54, or earlier in case of therapy discontinuation due to loss of response. FC levels were measured at baseline and at week 8 of treatment. The study primary aim was to assess whether FC levels at week 8 could predict mucosal healing at week 54. FC levels were measured at baseline and at week 8, with colonoscopy performed at week 54 or earlier if therapy was discontinued due to loss of response. Of the 97 patients included in the analysis, 26 experienced loss of response, while 71 (73%) with clinical response achieved clinical remission in 60 (61.9%) and mucosal healing in 45 (46.4%). FC levels at week 8 predicted mucosal healing at week 54 with a sensitivity of 75%, specificity of 88.9%, positive predictive value of 86.6%, and negative predictive value of 75.5%, based on a cut-off of 157.5 mg/kg. This study highlights FC as a promising early marker of therapeutic response in terms of mucosal healing, regardless of the biological therapy used.[79]

Linked color imaging (LCI) is useful tool for recognizing color differences in the mucosa, by facilitating the detection and recognition of colorectal neoplasms.[80]In the recent years there is data published showing the utility of LCI in the assessment of intestinal inflammation in UC patients. The study by Uchiyama et al. (2017) evaluated the efficacy of LCI in diagnosing mucosal inflammation and predicting relapse in UC patients in clinical remission. Fifty-two patients with UC, all in remission with a Lichtiger Colitis Activity Index (LCAI) ≤ 4, were enrolled, and 193 areas of colonic mucosa were assessed using the LASEREO endoscopic system (Fujifilm Co., Tokyo, Japan). LCI classified mucosal patterns into three categories: LCI-A (no redness), LCI-B (redness with visible vessels), and LCI-C (redness without visible vessels). Redness was quantified using the CIELAB color space, and histological inflammation was evaluated with the matts histopathological grading system. The study found excellent inter observer agreement for both LCI classification and the MES, with kappa values >0.8 between experts and non-experts. LCI was able to subdivide MES grades more precisely, with 46.4% of MES-0 areas showing redness (41.8% LCI-B and 4.6% LCI-C), and 60.5% of MES-1 areas classified as LCI-C. LCI classifications strongly correlated with histopathological findings, with higher matts grades observed in LCI-B and LCI-C areas. During the 30-month follow-up, 14 patients experienced relapse, of whom 64.3% were classified as LCI-C, 35.7% as LCI-B, and none as LCI-A, with LCI-A patients having significantly higher non-relapse rates ($p = 0.0055$). In contrast, MES did not significantly correlate with relapse ($p = 0.0632$). The LCI Index, measuring mucosal redness, was also significantly higher in relapsed patients (47.23) compared to non-relapsed patients (31.91) ($p = 0.0003$). The study concludes that LCI is a superior tool for assessing mucosal inflammation and predicting long-term outcomes compared to MES, and recommends further multi-center studies to validate these findings.[38]

Kanmura et al. (2019) conducted a pilot study to evaluate the diagnostic utility of LCI in assessing colonic mucosal inflammation in

UC. The study involved 21 UC patients, whose mucosal areas were examined using both conventional white-light imaging (WLI) and LCI using LASEREO system (Fujifilm Co., Tokyo, Japan) followed by biopsies from the regions of interest (ROI). The color values of the ROI were measured using the CIELAB color space system (L*, a*, and b* values), and these were correlated with endoscopic findings and histological activity, as determined by the Geboes index. The results demonstrated that the LCI-a and LCI-b color values were significantly higher in patients with active mucosal inflammation compared to those in remission ($p < 0.01$), while WLI color values showed no significant difference. Notably, only the LCI-a value was significantly correlated with the histological healing score, suggesting that LCI is a more sensitive tool for evaluating mucosal inflammation compared to WLI. The difference in color values (ΔE) between inflamed and non-inflamed mucosa was also significantly larger with LCI (ΔE = 7.1) than with WLI (ΔE = 3.1), highlighting LCI enhanced ability to visually differentiate inflammatory changes. The study concluded that LCI can reduce the need for invasive biopsies by providing a non-invasive, reliable method for detecting mucosal inflammation and assessing mucosal healing in UC.[81]

The study by Takagi et al. (2021) investigated the efficacy of LCI in predicting long-term outcomes in UC patients in remission, diagnosed with a MES of 0. A total of 26 patients were enrolled, and their colonic mucosa was evaluated using the LASEREO endoscopic system (Fujifilm Co., Tokyo, Japan). LCI images were classified into LCI-A (no redness), LCI-B (redness with visible vessels), and LCI-C (redness without visible vessels). Histological activity was assessed using the Geboes score, with active mucosal inflammation defined as Geboes > 2B.1. Over a 48-month follow-up, none of the LCI-A patients relapsed, while 47.1% of LCI-B patients experienced relapse ($p = 0.018$). This indicated that LCI was more effective in predicting relapse than MES. Furthermore, 34.6% of MES 0 patients were classified as LCI-A, and 65.4% as LCI-B, showing LCI's ability to subdivide MES 0 into more precise categories. While histological findings based on the Geboes

score did not significantly correlate with relapse (p = 0.529), LCI-B patients tended to have higher Geboes scores, suggesting LCI may detect subtle mucosal changes not identified by histology. The study demonstrated excellent inter-observer agreement for LCI classification (kappa = 0.857), supporting its reliability. Overall, the results suggest LCI provides a more sensitive and accurate method for predicting relapse and assessing mucosal healing in UC patients.[82]

Kanmura et al. (2020) also conducted a study to evaluate the correlation between LCI findings and the clinical relapse rate in UC patients, particularly focusing on the LCI-scarlet color lesion. This retrospective study analyzed 58 UC patients (22 females, 36 males, median age 47.2 years) who underwent colonoscopy between August 2016 and October 2018 at Kagoshima University Hospital, all of whom had MES of 0 or 1. LCI was used alongside WLI to assess the orange-like LCI-scarlet color lesion, which emphasizes redness and yellowness. During the 1-year follow-up period, clinical relapse, defined as the need for intensified treatment, was observed in 12 patients (20.1%). Among them, 83.3% had LCI-scarlet color lesions, compared to 63% of the clinical remission group, which had no LCI-scarlet color lesions. There was a significant association between the presence of LCI-scarlet color lesions and clinical relapse (p = 0.002). In MES 0 patients, 100% of those with LCI-scarlet color lesions relapsed, while 40% of MES 1 patients with LCI-scarlet color lesions relapsed. The Kaplan-Meier analysis confirmed that patients with LCI-scarlet color lesions had a significantly higher relapse rate than those without (p = 0.02). Multivariate analysis showed that the LCI-scarlet color lesion was an independent predictor of clinical relapse (odds ratio, 14.8; 95% CI, 1.68–130.4; p < 0.015). In contrast, there was no significant difference in relapse rates between MES 0 and MES 1 groups based on WLI (p = 0.063). The study concluded that LCI-scarlet color lesions are highly predictive of clinical relapse in UC patients, making LCI a useful tool for assessing mucosal healing and guiding clinical management in UC. The study emphasized the need for larger-scale

prospective research to further validate the diagnostic utility of LCI in predicting UC relapse.[83]

The study, conducted by Matsumoto K. et al. (2020), investigated the clinical utility of LCI for evaluating endoscopic activity and predicting relapse in UC patients and enrolled 72 consecutive UC patients in remission who underwent colonoscopy at the institution between September 2016 and October 2018. The study examined the correlation between redness observed in WLI and LCI, and histopathological inflammation (Geboes score: GS) at 238 biopsy sites. Patients were classified into three groups based on WLI/LCI findings: A (WLI-/LCI-), B (WLI-/LCI+), and C (WLI+/LCI+). The relationship between WLI/LCI classification and relapse was assessed in 64 patients followed up for more than 12 months and compared to the MES. Results showed that a GS of 0 or 1 was present in 89% of WLI/LCI non-redness sites, while a GS of 2 or 3 was found in 42% of WLI non-redness/LCI redness sites. LCI findings were significantly correlated with GS. During follow-up, 10 patients in group C and four patients in group B relapsed, but none in group A. Non-relapse rates were significantly correlated with WLI/LCI classification, but not with MES. Matsumoto K. concluded that LCI is a valuable tool for accurately assessing endoscopic activity and predicting relapse in UC by detecting mild inflammation that is unrecognizable by WLI.[84]

Achieving endoscopic remission is a key therapeutic goal in UC. While the MES using white light imaging is commonly employed to evaluate endoscopic findings, LCI has shown promise. The study, conducted by Saito D. et al.(2023), aimed to evaluate the correlation between LCI and histopathological findings and to establish a new LCI endoscopic evaluation index for UC. The study was conducted at Kyorin University, Kyoto Prefectural University, and Fukuoka University Chikushi Hospital. Ninety-two UC patients with a MES ≤1 in clinical remission who underwent colonoscopy were included. The LCI index was defined using three parameters: redness (R) graded 0-2, area of inflammation (A) graded 0-3, and lymphoid follicles (L) graded 0-3. Histological healing was defined as a Geboes score <2B.1. Central judgment was

used to determine endoscopic and histopathological scores. In 92 patients, 85 biopsies from the sigmoid colon and 84 biopsies from the rectum (total 169 biopsies) were evaluated. The distribution of grades in the LCI index-R was 22 (Grade 0), 117 (Grade 1), and 30 (Grade 2). For LCI index-A, there were 113 (Grade 0), 34 (Grade 1), 17 (Grade 2), and 5 (Grade 3) cases. For LCI index-L, there were 124 (Grade 0), 27 (Grade 1), 14 (Grade 2), and 4 (Grade 3) cases. Histological healing was observed in 84.0% of the cases (142 of 169), with significant associations between histological healing or non-healing and LCI index-R (P=0.013) and LCI index-A (P=0.0014). The new LCI index developed by Saito D. et al. is useful for predicting histological healing in UC patients with MES ≤1 and clinical remission.[85]

The prospective study by Patel M. et al.(2022) evaluated the use of LCI on the Fujifilm EluxeoTM platform to predict mucosal healing and inflammation in ulcerative colitis (UC) patients, aiming to provide a less expensive and quicker alternative to conventional biopsies, which require experienced histopathologist and can delay treatment decisions. The study enrolled 110 UC patients at a tertiary-care institution, all undergoing routine endoscopic assessment. Participants provided a fecal calprotectin sample within seven days prior to endoscopy and completed the simple clinical colitis activity index (SCCAI). During endoscopy, the MES was recorded. Video recordings and still images using WLE and LCI, along with paired biopsies from the most inflamed region or rectum if the participant was in endoscopic remission (MES 0), were obtained. Histology was graded using the Nancy Histology Index (NHI) by a blinded pathologist. Optical biopsies (50 x 50 pixels) corresponding to the tissue biopsy sites on LCI and WLE were analyzed using the international commission of illumination (CIELAB) colour-space for L* (lightness), a* (red-green), and b* (blue-yellow) values. The study's participants included 49 females, with a mean age of 39.9 years (±13.4), 40.9% having extensive disease distribution, a median SCCAI of 3.0 (IQR = 6.0), and a median calprotectin of 306.0 (IQR = 630.3). MES distribution was 0 = 27.3%, 1 = 20.9%, 2 = 39.1%, and 3 = 12.7%. NHI grading distribution was 0 =

26.4%, 1 = 5.5%, 2 = 20.0%, 3 = 32.7%, and 4 = 15.5%. The a* value in LCI emerged as the best predictor for inflammation, significantly lower for mucosal healing (NHI 0) than active disease (NHI > 0), with values of 15.2±9.9 versus 37.2±10.3, $p<0.001$, and high accuracy (AUROC = 0.92), superior to WLE optical biopsy (AUROC = 0.79). Strong positive associations were found between a* values and NHI grading ($r = 0.68$, $p<0.0001$), calprotectin ($r = 0.53$, $p<0.0001$), and MES ($r = 0.66$, $p<0.0001$), comparable to NHI correlations with calprotectin ($r = 0.53$, $p<0.0001$) and MES ($r = 0.71$, $p<0.0001$). The study concludes that LCI optical biopsy accurately predicts mucosal healing and inflammation severity on histology, offering potential to replace conventional biopsies, thereby improving patient care and reducing demands on pathology services.[86]

MATERIAL AND METHODS

The study on “Mucosal healing in Ulcerative colitis: A correlation study between white light endoscopy, linked color imaging and histology” was conducted in department of gastroenterology at Dayanand medical college and hospital (DMCH) Ludhiana. DMCH is a more than 1600 bedded tertiary care hospital in north Indian state of Punjab. An approval to conduct the study was obtained from institutional ethical review board. The study did not involve any diagnostic or therapeutic maneuver outside the routine evaluation of these patients and did not entail any extra costs to them.

Study site

All the patients with ulcerative colitis in symptomatic remission who attended the gastroenterology out-patient department at Dayanand Medical College and Hospital, Ludhiana, Punjab, India between January 1, 2023 and December 31, 2023.

Duration of Study

One year from 1st January 2023 till 31st December 2023.

Study Design

The study design is prospective.

Inclusion criteria

- Adults (>18 years of age) with established ulcerative colitis in symptomatic remission were enrolled.
- Symptomatic remission was defined as normal stool frequency and no bleeding per rectum, and normal physician global assessment as depicted by partial Mayo clinic score of 0-1.[87]

Exclusion Criteria

Patients with ulcerative colitis with:

- Clinically active disease (defined as partial Mayo clinic score >1)
- Infectious colitis
- Severe co-morbid cardiovascular, pulmonary, renal or neurological illness.
- Pregnancy and lactation.

Study Protocol

A total of 103 patients were enrolled in this study. Written informed consent were taken from all the patients. All patients were evaluated prospectively as per standard protocol including history, clinical examination and laboratory investigations. The history focused on the information about the demographics, background information about ulcerative colitis were noted including duration of disease, extent of ulcerative colitis, clinical course, and treatment taken including biologics therapy. Specific inquiries about presence of co-morbid condition (hypertension, hypothyroidism, hyperthyroidism, diabetes mellitus, cardiovascular disease etc.) were made. Inquiries about smoking, alcohol and any other drug use habit were made. Clinical examination included a general physical examination including pulse, blood pressure, respiratory rate, anthropometry, mid upper arm circumference and hand grip with dynamometer were recorded. Family history was also noted for any inflammatory bowel disease. The laboratory investigations included routine investigations like hemogram, serum albumin, inflammatory marker like ESR, CRP and fecal calprotectin were done after taking due precautions while taking samples. All the patients were in symptomatic remission and off steroids for more than three months and fecal calprotectin were done within 1 week before colonoscopy or sigmoidoscopy.

All patients were given routine bowel preparation with two liters of polyethylene glycol 3350, sodium chloride, sodium hydrogen carbonate and potassium chloride concentrate for oral solution. A high definition EC-762P-V/L endoscope were used as part of the endoscopic system that consists of VP-7000 processor and BL-7000 light source (Fujifilm Medical Co., Tokyo, Japan) in all colonoscopy/sigmoidoscopic examinations. This endoscopic system is capable of producing light suitable for white light imaging and linked color imaging. Colonoscopy/sigmoidoscopic examination were performed by one experienced endoscopist. The endoscopic images with WLI and LCI were captured from the same position in a row before biopsy, then the biopsy were performed targeting the reddest site in the observed area

and rectum if normal mucosal study. In each case MES[14] and UCEIS[15] were evaluated under WLI observation. Endoscopic LCI images were separated into three subgroups (A-no redness, B-redness with visible vessels, C- redness without visible vessels). The endoscopic images obtained by WLI and LCI before the biopsy were analyzed. The redness of the lesion in the region of interest (ROI) was quantified using digital image analysis. A ROI was selected from the endoscopic image, corresponding to the area where biopsies were performed. Using Photoshop CS6 (Adobe system Inc.), the Lab numerical values of the ROI were analyzed and converted to the CIELAB color space, which closely resembles human visual perception. The a* value, a component of the CIELAB color space, was used as an objective measure of redness, providing an LCI-index that assesses the degree of inflammation. The formula used for conversion from Photoshop's 'a' value to CIELAB 'a*' value was: CIELAB 'a*' = (Photoshop 'a' / 128) × 120. In essence, this calculation is a linear transformation that maps the Photoshop 'a' value to the CIELAB 'a*' value, preserving the color position on the red-green axis.

The histological examination of all the biopsy specimens was performed by an experienced pathologist who was blinded to the patient's endoscopic activity. The histological assessment was based on Nancy index - Grade 0 = No histological significant disease; Grade 1 = Chronic inflammatory infiltrate with no acute inflammatory infiltrate; Grade 2 = Mild active disease; Grade 3 = Moderately active disease; Grade 4 = Severely active disease. Histological remission was defined by nancy histological index grade 0.[88]

Statistical Analysis

Data were described in terms of range; mean ±standard deviation (± SD), median (IQR), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Kruskal-Wallis Test. For comparing categorical data, Chi square ($\chi 2$) test was performed and fisher exact test was used when the expected frequency is less than 5. Correlation coefficients was calculated by a

Spearman’s rank correlation analysis. The discriminatory power of each putative marker was described using the receiver operating characteristics area under curve (ROC-AUC).Sensitivity, specificity, accuracy, positive predictive value, and negative predictive value was calculated. Kappa value was calculated to find the agreement between the variables. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21.0 version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATION AND RESULTS

In this study, we analyzed the data of 103 patients of ulcerative Colitis who fulfilled the inclusion criteria from 1st January 2023 to 31st December 2023.

The study included 103 patients with ulcerative colitis, with a diverse age distribution as shown in Table-1. The majority of patients were between 31-40 years (28.8%), followed by those under 30 years (28.2%), 41-50 years (22.3%), and over 50 years (21.4%).

Table 1: Age distribution of Study Patients (n=103)

Age groups (in years)	No. of cases (%)
< 30	29 (28.2)
31-40	29 (28.8)
41-50	23 (22.3)
> 50	22 (21.4)

The age distribution of the study patients is illustrated in Figure 1. The chart reveals a relatively even distribution across the age groups, with a slight peak in the 31-40 year range (28.8%).

The gender distribution of the study patients is summarized in Table 2 and Figure 2. The table and pie chart reveals a female predominance, with 62.1% (n=64) of patients being female, compared to 37.9% (n=39) male patients.

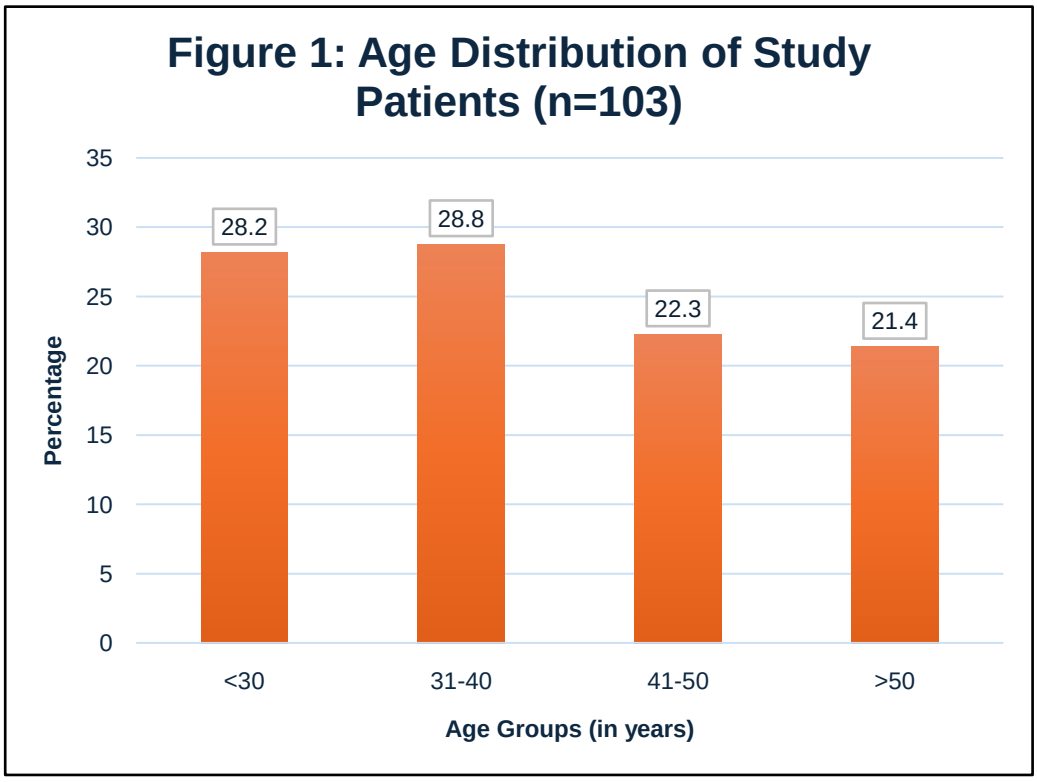
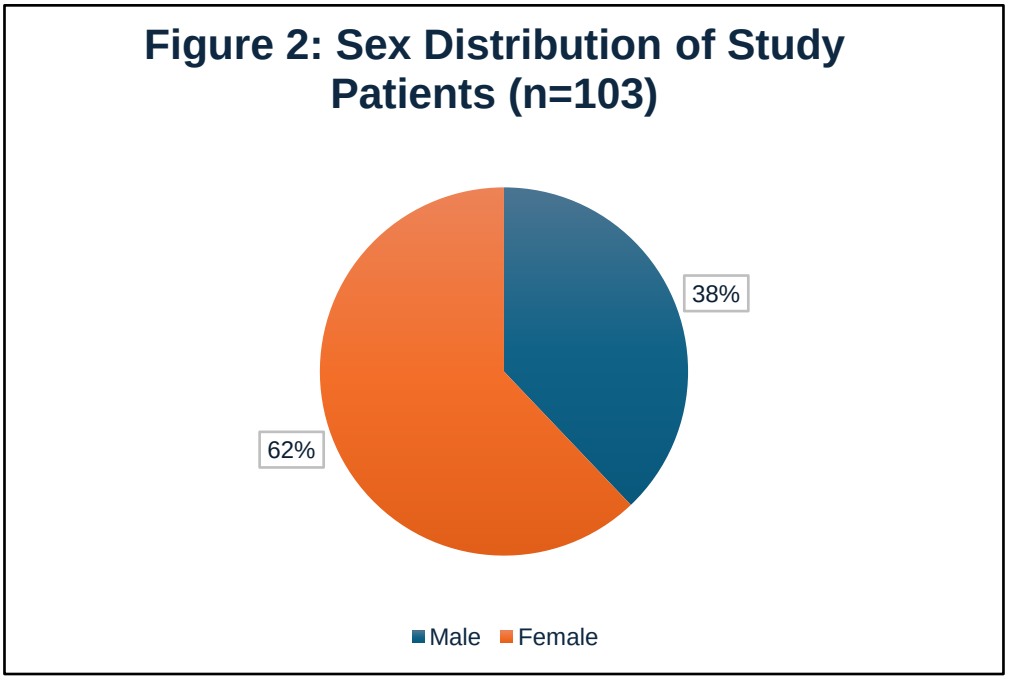


Figure 1: Age Distribution of Study Patients (n=103)
35
30
25
20
15
10
5
0
Percentage
28.2
28.8
22.3
21.4
<30
31-40
41-50
>50
Age Groups (in years)

Table 2: Gender distribution of study patients (n=103)	
Sex	No.of cases (%)
Male	39 (37.9)
Female	64 (62.1)



The demographic and clinical characteristics of the study patients at baseline are presented in Table 3. The table shows that the mean age of the patients was 39 years. The mean age at onset of symptoms was 31.8 years, while the mean age at diagnosis was 32.5 years. The mean disease duration was 7.3 years. Additionally, the mean diagnostic delay duration was 0.7 years, indicating a delay of approximately 8 months from symptom onset to diagnosis.

Table 3: Baseline characteristics of Study Patients (n=103)	
Parameter	Mean± SD
Age (in years)	39 ± 12
Age at onset of symptom (in years)	31.8 ± 11.7
Age at diagnosis (in years)	32.5 ± 11.7
Duration of disease (in years)	7.3 ± 6.4

The extent of disease in the study patients was noted, with the majority (68.9%) having left-side colitis (E2), followed by proctitis (E1) in 19.4% of patients, and pan-colitis (E3) in 11.7% of patients. This distribution is illustrated in Table 4 and a pie chart (Figure 3) showing the proportion of patients with each disease extent. The predominance of left-side colitis suggests that this subtype is the most common manifestation of the disease in the study patients, while the presence of proctitis and pan-colitis highlights the variability in disease extent.

Table 4: Extent of disease in Study Patients (n=103)	
Disease Extent	No. of cases (%)
Proctitis (E1)	20 (19.4)
Left sided colitis (E2)	71 (68.9)
Pan-colitis (E3)	12 (11.7)

The anthropometric measurements revealed a mean weight of 65.2 kg (range: 36.7-108 kg), mean height of 167.4 cm (range: 147-183 cm), mean BMI of 23.2 kg/sq^2 (range: 14.9-34 kg/sq^2), mean MUAC of 28.9 cm (range: 18-32 cm), and mean hand grip strength of 29.7 kg (range: 11-56 kg) as shown in Table 5.

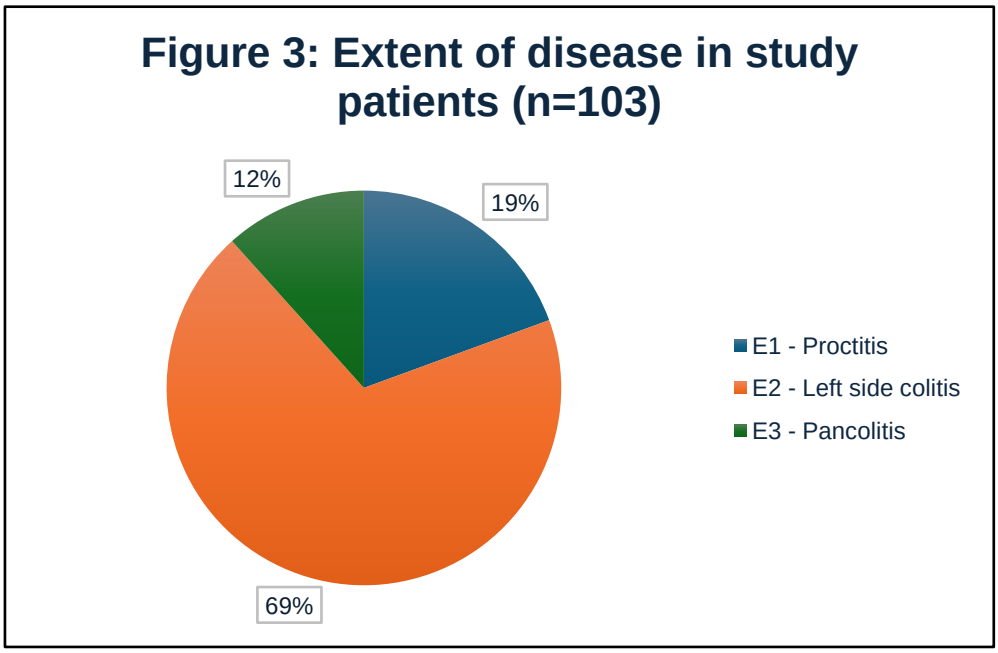


Table 5: Anthropometry of Study Patients (n=103)	
Parameter	Mean ± SD
Weight (in Kg)	65.2 ± 13
Height (in cm)	167.4 ± 9
BMI (in kg/sq^2)	23.2 ± 4
MUAC (in cm)	28.9 ± 2.5
Hand grip strength (in Kg)	29.7 ± 9.9

As depicted in Table-6, the laboratory results of the study patients showed a range of values for various parameters. Hemoglobin levels had a mean of 12.3 gm/dl, with a range of 8.9 to 16.4 gm/dl, indicating some patients had mild anemia. The packed cell volume (PCV) had a mean of 38%, with a range of 28.1 to 48.9%, and mean corpuscular volume (MCV) had a mean of 84.3 fl, with a range of 68.6 to 109.0 fl. total leukocyte count (TLC) had a mean of 6.7 x 1000/microltr, with a range of 4.1 to 10.8 x 1000/microltr, and platelet count had a mean of 233.1 x 1000/microltr, with a range of 49 to 456.0 x 1000/microltr. erythrocyte sedimentation rate (ESR) had a mean of 11.5 mm/1st hour, with a range of 2 to 26.0 mm/1st hour, and C-reactive protein (CRP) had a mean of 2.8 mg/l, with a range of 0.1 to 12.0 mg/l. Fecal calprotectin (FC) had a mean of 88.8 mcg/gm, with a range of 25 to 2000.0 mcg/gm, indicating some patients had elevated levels. Albumin levels had a mean of 3.8 gm/dl, with a range of 2.9 to 4.9 gm/dl.

Table 6: Laboratory parameter of Study Patients (n=103)		
Parameter	Mean ± SD	Mode
Hemoglobin (gm/dl)	12.3 ± 1.8	12.1
PCV (%)	38 ± 5.1	38.1
MCV (fl)	84.3 ± 7.1	83.8
TLC (1000/ul)	6.7 ± 1.6	6.8
Platelets (1000/ul)	233.1 ± 75.8	209
ESR (mm1st-hour)	11.5 ± 6.7	10
CRP (mg/lt)	2.8 ± 2.7	1.7
Fecal Calprotectin (mcg/gm)	88.8 ± 207	28
Albumin (gm/dl)	3.8 ± 0.5	3.9

The study patients had various co-morbidities, including hypertension (3.9%, n=4), diabetes mellitus (1.9%, n=2), hypothyroidism (2.9%, n=3), coronary artery disease (2.9%, n=3), and cerebrovascular disease (1%, n=1). The majority of patients did not have any of the listed co-morbidities (Figure 4 and Table-7).

Table 7: Co-morbidities of Study Patients (n=103)	
Comorbidity	No. of patients (%)
Hypertension	4 (3.9)
Diabetes mellitus	2 (1.9)
Hypothyroidism	3 (2.9)
Coronary artery disease	3 (2.9)
Cerebrovascular disease	1 (0.97)

The study patient's habits regarding alcohol and smoking were noted, revealing that only a small proportion engaged in these behaviors. Specifically, merely two patients consumed alcohol, while a vast majority of 98% (n=101) did not. Similarly, only one patient had history of smoking, whereas an overwhelming 99% (n=102) did not(Table 8).

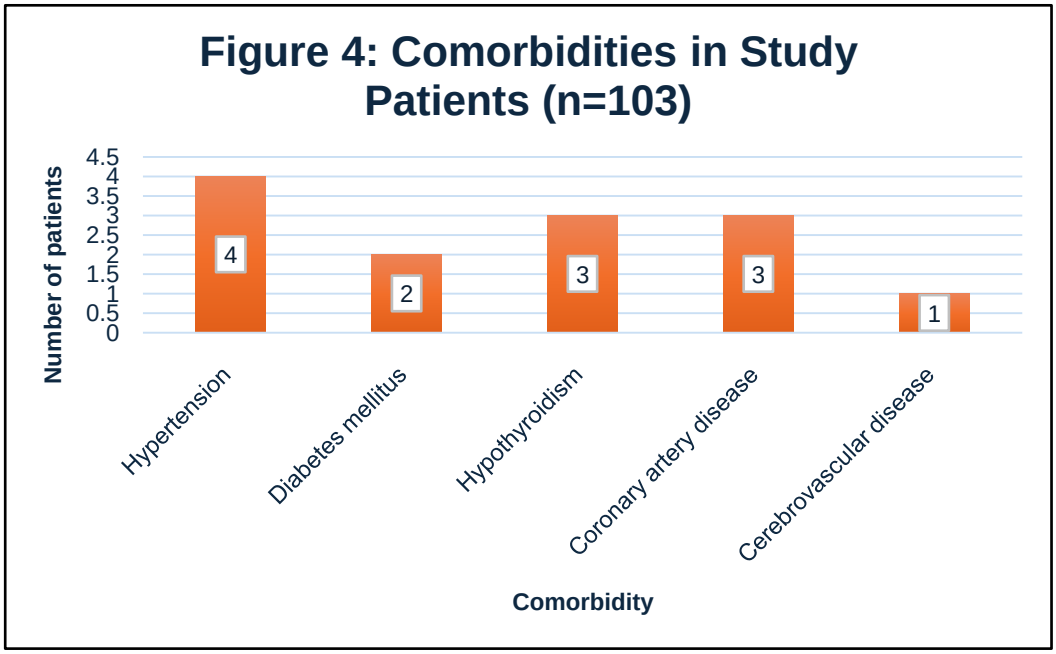


Table 8: Alcohol and Smoking habits in Study Patients (n=103)	
Parameter	No. of patients
Alcohol	2
Smoking	1

A small proportion of the study patients had a family history of Inflammatory Bowel Disease (IBD), with only 3 patients (2.9%) reporting a positive family history, while the vast majority of 100 patients (97.1%) did not have a family history of IBD. This suggests that the majority of the study patients did not have a genetic predisposition to IBD, and other factors may have played a more significant role in the development of the disease in this population.(Table 9).

Table 9: Family history of IBD in Study Patients	
Family History of IBD	No. Of cases (%)
Yes	3 (2.9)
No	100 (97.1)

The study patients had various treatment histories, with all 103 patients (100%) having received oral 5-ASA (5ASA-O) therapy. Additionally, 24 patients (23.3%) had been treated with azathioprine, 2 patients (1.9%) with 6-MP, 35 patients (34%) with tofacitinib (Tofa), and 1 patient (0.97%) with infliximab therapy. Furthermore, 40 patients (38.8%) had received oral steroid therapy, 4 patients (3.9%) had undergone fecal microbiota transplantation (FMT), and 4 patients (3.9%) had received rectal steroid therapy. Notably, 51 patients (49.5%) had received rectal 5-ASA therapy (5ASA-R). This diversity in treatment histories suggests that the study patients had varied responses to different therapies, highlighting the complexity of managing IBD.(Table 10 & Figure 5). Figure 6 also shows current treatment in study patients.

Table 10: Current and Past treatment in Study Patients (n=103)	
Drugs	No. of cases (%)
5 ASA (Oral)	103 (100)
Thiopurines	26 (25.2)
Tofacitinib	35 (34)
Biologics	1 (0.97)
Steroid (Oral)	40 (38.8)
FMT	4 (3.9)
Steroid(Rectal)	4 (3.9)
5-ASA(Rectal)	51 (49.5)

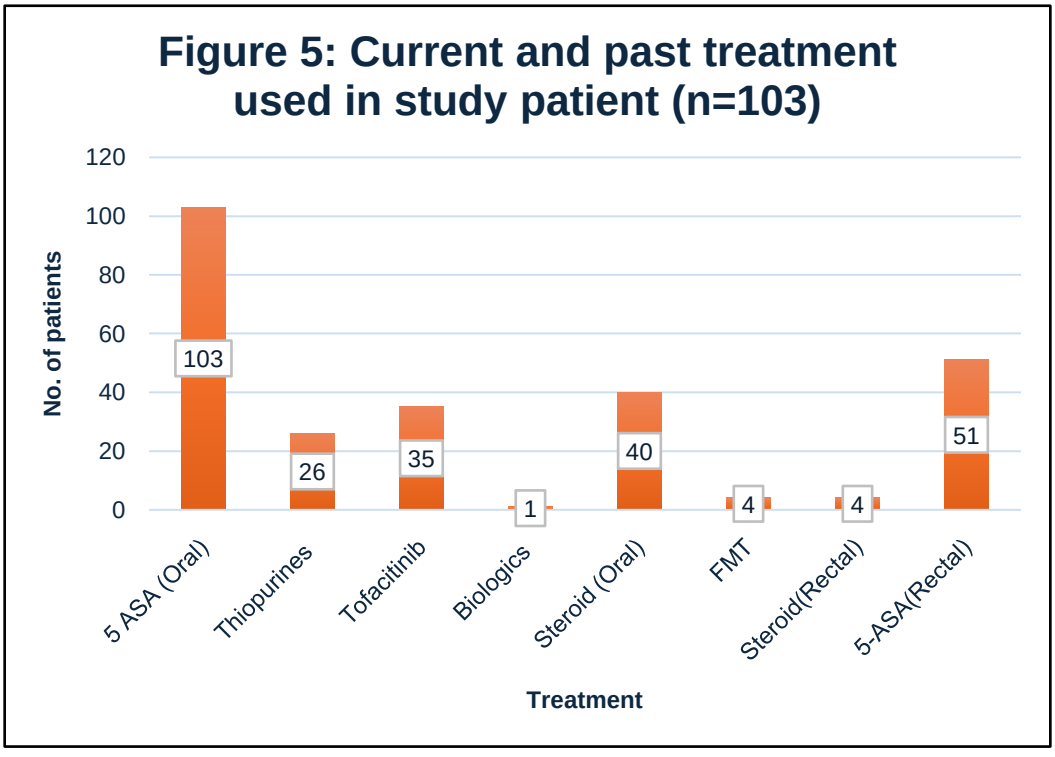


Figure 6: Current treatment in Study Patients (n=103)

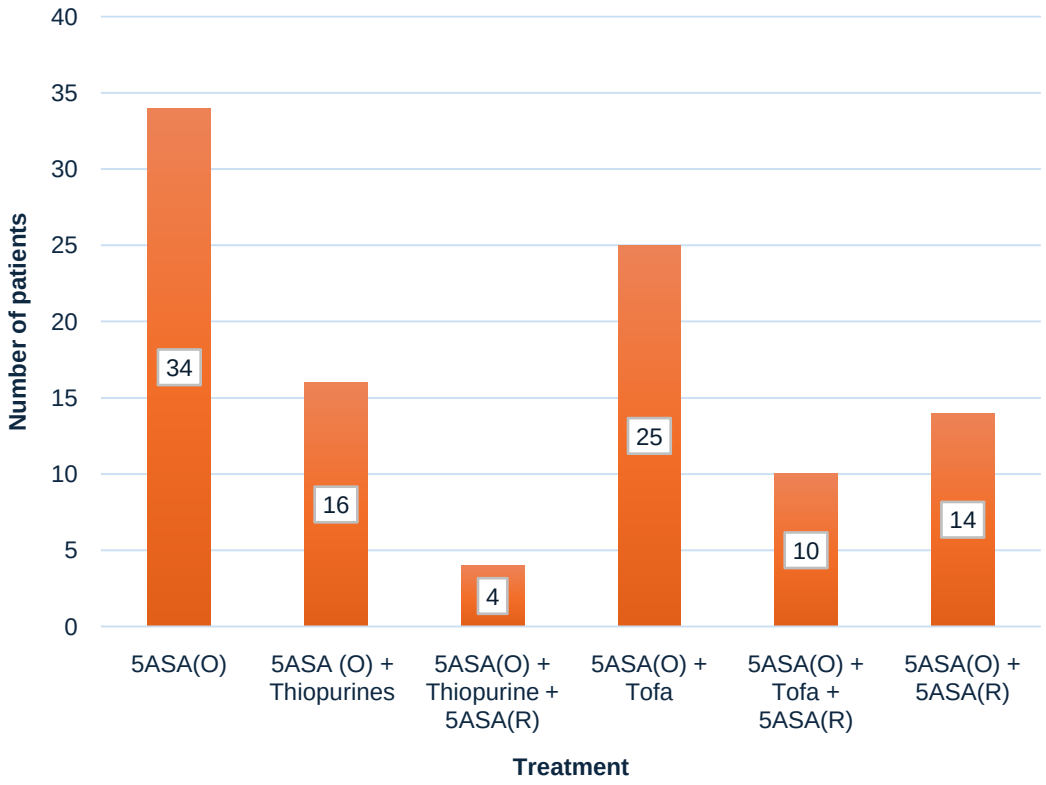


Table 11: Partial Mayo score of Study Patients (n=103)	
PMS	No. of cases (%)
0	88 (85.4)
1	15 14.6)

All 103 study patients were in symptomatic remission in accordance to Partial Mayo Score. Eighty eight patients had PMS-0 (85.4%) fifteen patient had PMS-1 (14.6%). (Table 11).

Table 12: White light endoscopy (MES) of Study Patients (n=103)	
MES	No. of patients (%)
0	66 (64.1)
1	25 (24.3)
2	8 (7.8)
3	4 (3.9)

White light endoscopy was performed on all 103 study patients, and the results were categorized based on the mayo endoscopic score (MES). Sixty six patients (64.1%) had an MES of 0 and 25 patients (24.3%) had an MES of 1indicating mucosal healing, while 8 patients (7.8%) had an MES of 2 and 4 patients (3.9%) had an MES of 3.(Table 12 & Figure 7).

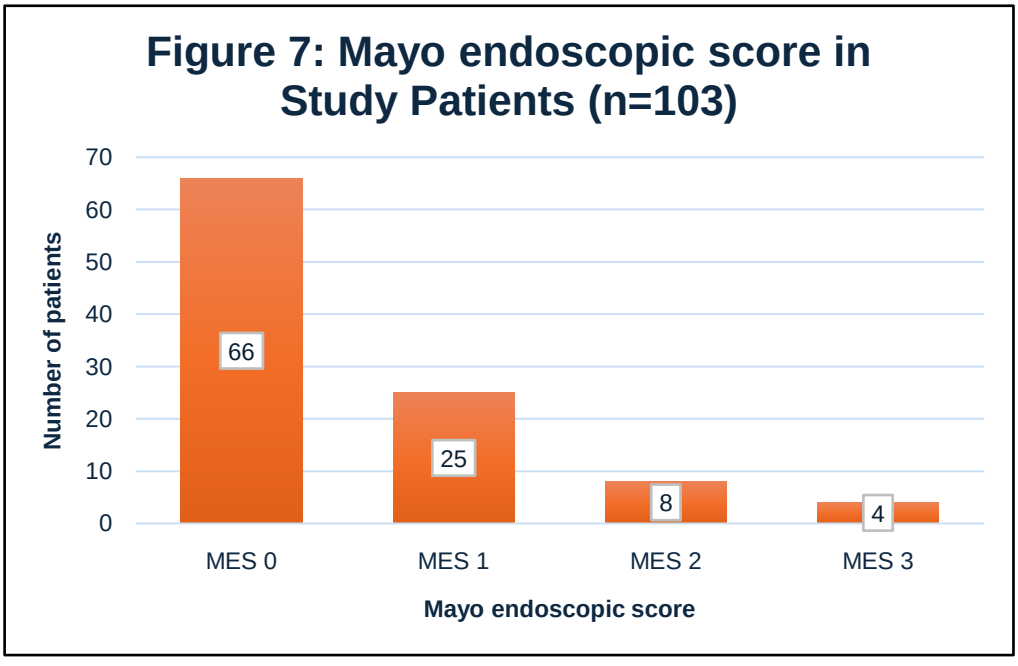


Table 13: White light endoscopy (UCEIS) of Study Patients (n=103)	
Score	No. of patients (%)
UCEIS 0	63 (61.2)
UCEIS 1	21 (20.4)
UCEIS 2	7 (6.8)
UCEIS 3	5 (4.9)
UCEIS 4	2 (1.9)
UCEIS 5	5 (4.9)
UCEIS 6	0 (0)
UCEIS 7	0 (0)
UCEIS 8	0 (0)

The Ulcerative colitis endoscopic index of severity (UCEIS) scores were also assessed in all 103 study patients, revealing a range of endoscopic disease severity. The majority of patients (n=63) had a UCEIS score of 0. A significant proportion (n=21) had a UCEIS score of 1, while 7 patients had a UCEIS score of 2. Five patients having a UCEIS score of 3, two patients having a UCEIS score of 4, and five patients having a UCEIS score of 5, none had score more than 5 (Table 13 & Figure 8).

Figure 8: Ulcerative colitis endoscopic index of severity (UCEIS) in Study Patients (n=103)

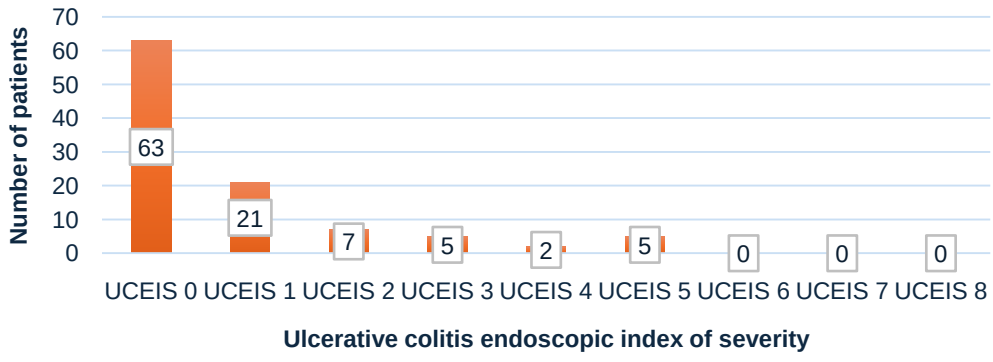


Table 14: Linked color imaging in Study Patients (n=103)	
Category	No. of patients (%)
LCI A	58 (56.3)
LCI B	25 (24.3)
LCI C	20 (19.4)

Linked color imaging (LCI) was performed on all 103 study patients, and the results were categorized into three groups. The majority of patients (n=58) were classified as LCI A, indicating no mucosal redness and normal vascular pattern. A significant proportion (n=25) were classified as LCI B, indicating mucosal redness and preserved vascular pattern, while 20 patients were classified as LCI C, indicating mucosal redness and obliterated vascular pattern. These findings suggest that LCI can help identify varying degrees of mucosal inflammation in patients with ulcerative colitis, even in those with symptomatic remission(Table 14 & Figure 9).

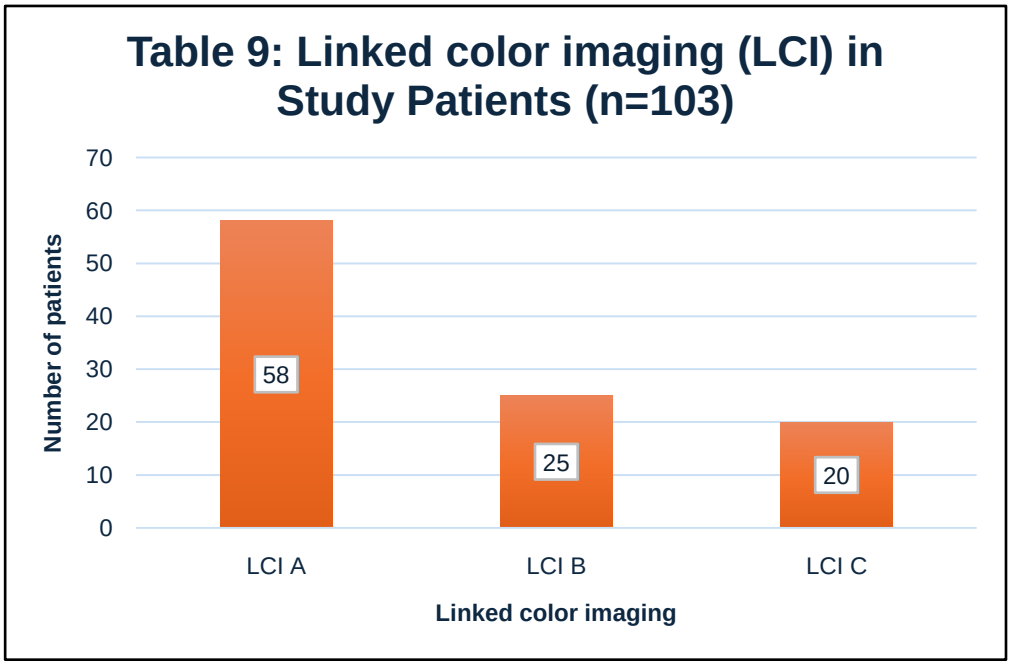


Table 15: Histological disease activity in Study Patients (n=103)	
Nancy Histological Index	No. of patients (%)
NHI 0	51(49.5)
NHI 1	18 (17.5)
NHI 2	5 (4.9)
NHI 3	23 (22.3)
NHI 4	6 (5.8)

Histological disease activity was assessed in all 103 study patients using the Nancy Histological Index (NHI). The results showed that 51 patients (49.5%) had an NHI score of 0, indicating no histological evidence of disease activity or histological remission. In contrast, 52 patients (50.5%) had an NHI score of 1 or higher, indicating active histological disease. Of these, 18 patients (17.5%) had an NHI score of 1, five patients (4.9%) had an NHI score of 2, twenty three patients (22.3%) had an NHI score of 3, and six patients (5.8%) had an NHI score of 4. These findings suggest that approximately half of the patients had active histological disease, despite being in symptomatic remission. (Table 15 & Figure 10)

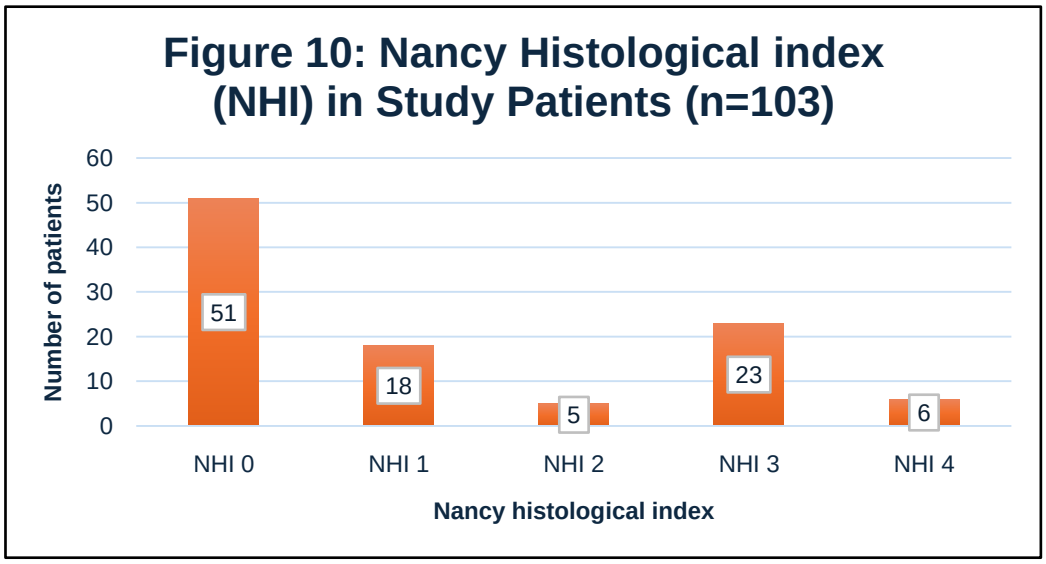


Figure 10: Nancy Histological index (NHI) in Study Patients (n=103)
Number of patients
60
50
40
30
20
10
0
51
18
5
23
6
NHI 0
NHI 1
NHI 2
NHI 3
NHI 4
Nancy histological index

Table 16: Distribution and Correlation between MES and LCI in Study Patients (n=103)						
	LCI A	LCI B	LCI C	Total	Spearman's rho	p-value
MES 0	50	16	0	66	0.673	<0.001
MES 1	8	9	8	25		
MES 2	0	0	8	8		
MES 3	0	0	4	4		
Total	58	25	20	103		

Table-16 presents the distribution of LCI among MES subgroups. The majority of patients with MES-0 had LCI A (50/66), LCI B (16/66) and none had LCI C. Linked color imaging has further divided MES-1 in LCI A(8/25), LCI B(9/25) and LCI C(8/25). All patients with MES-2 and MES-3 had LCI C (12/12). The data also reveals a significant correlation between linked color imaging and mayo endoscopic score (spearman's rho=0.673, p-value<0.001). The distribution of LCI among MES subgroup is shown in the Figure-11.

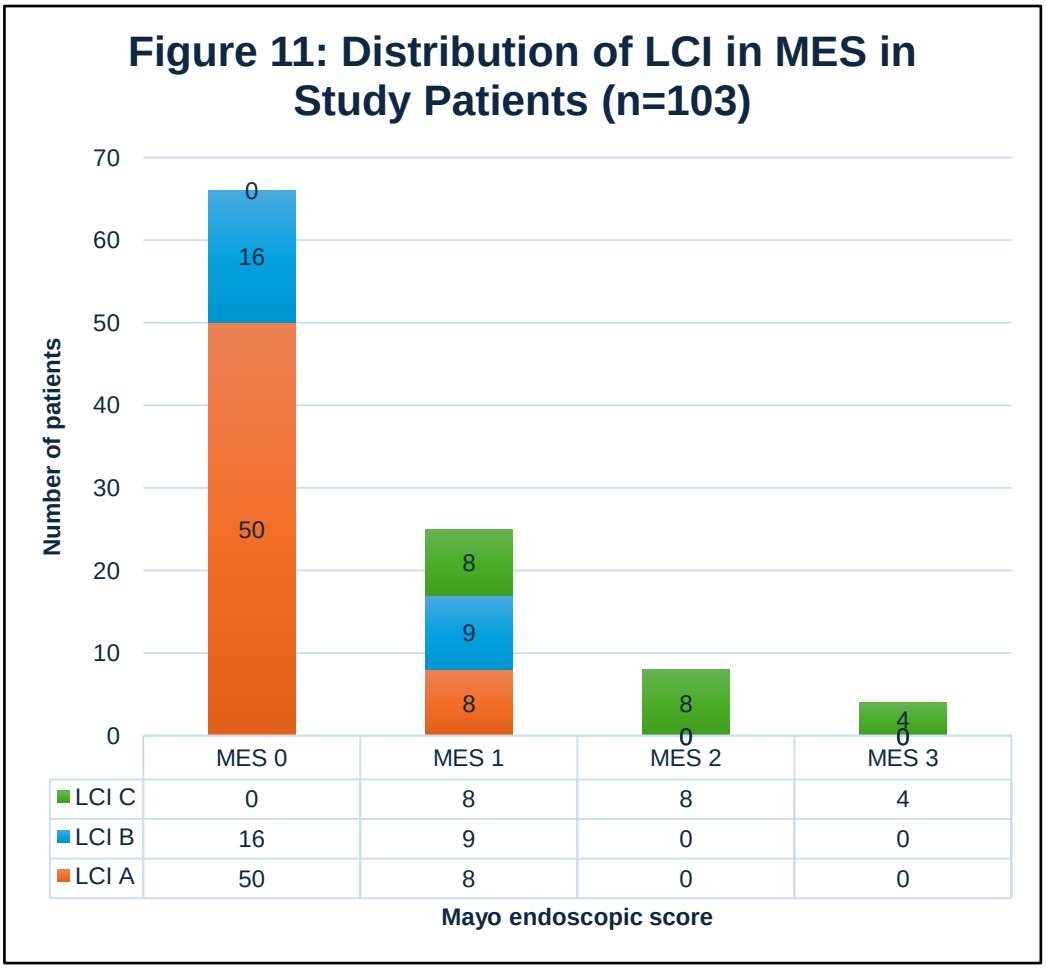
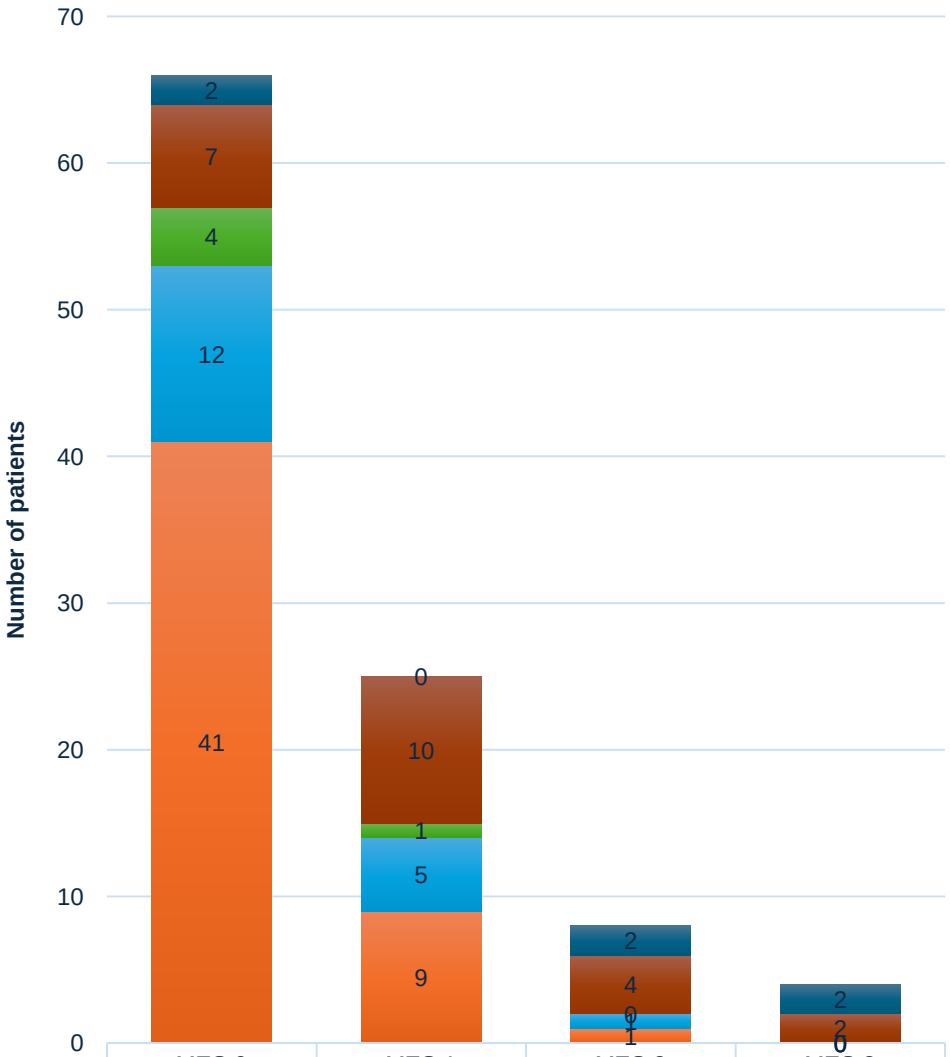


Table 17: Distribution and Correlation between MES and NHI (n=103)							
	MES 0	MES 1	MES 2	MES 3	Total	Spearman's rho	p-value
NHI 0	41	9	1	0	51	0.449	<0.001
NHI 1	12	5	1	0	18		
NHI 2	4	1	0	0	5		
NHI 3	7	10	4	2	23		
NHI 4	2	0	2	2	6		
Total	66	25	8	4	103		

Table-17 presents the distribution of NHI among MES subgrous. The majority of patients in endoscopic mucosal remission as per white light endoscopy, that is, MES-0 had histological remission, NHI-0 (41/66). However significant number of patients had histologically active disease, such as NHI-1 (12/66), NHI-2 (4/66), NHI-3 (7/66) and NHI-4 (2/66). Likewise significant number of patients in MES-1, which was previously counted as criteria for mucosal healing or remission, had histologically active disease. Out of 25 patients in MES-1 subgroup only nine had histological remission that is NHI-0, however NHI-1 was seen in 5/25, NHI-2 in 1/25, NHI-3 in 10/25 and none had NHI-4. Out of eight patients with MES-2 only one was in histological remission (NHI-0 in 1/8) and other seven had histologically active disease (NHI-1 in 1/8, NHI-3 in 4/8, NHI-4 in 2/8) and none had NHI-2. All patient with MES-3 had histologically active disease (NHI-3 in 2/4 and NHI-4 in 2/4). The data reveals a moderate correlation between MES and NHI (Spearman's rho=0.449, p-value < 0.001). The total distribution of NHI among MES subgroups is shown in the figure-12. These findings suggest that MES is a useful predictor of histological disease activity in patients with ulcerative colitis.

Figure 12: Distribution of NHI in MES in Study Patients (n=103)



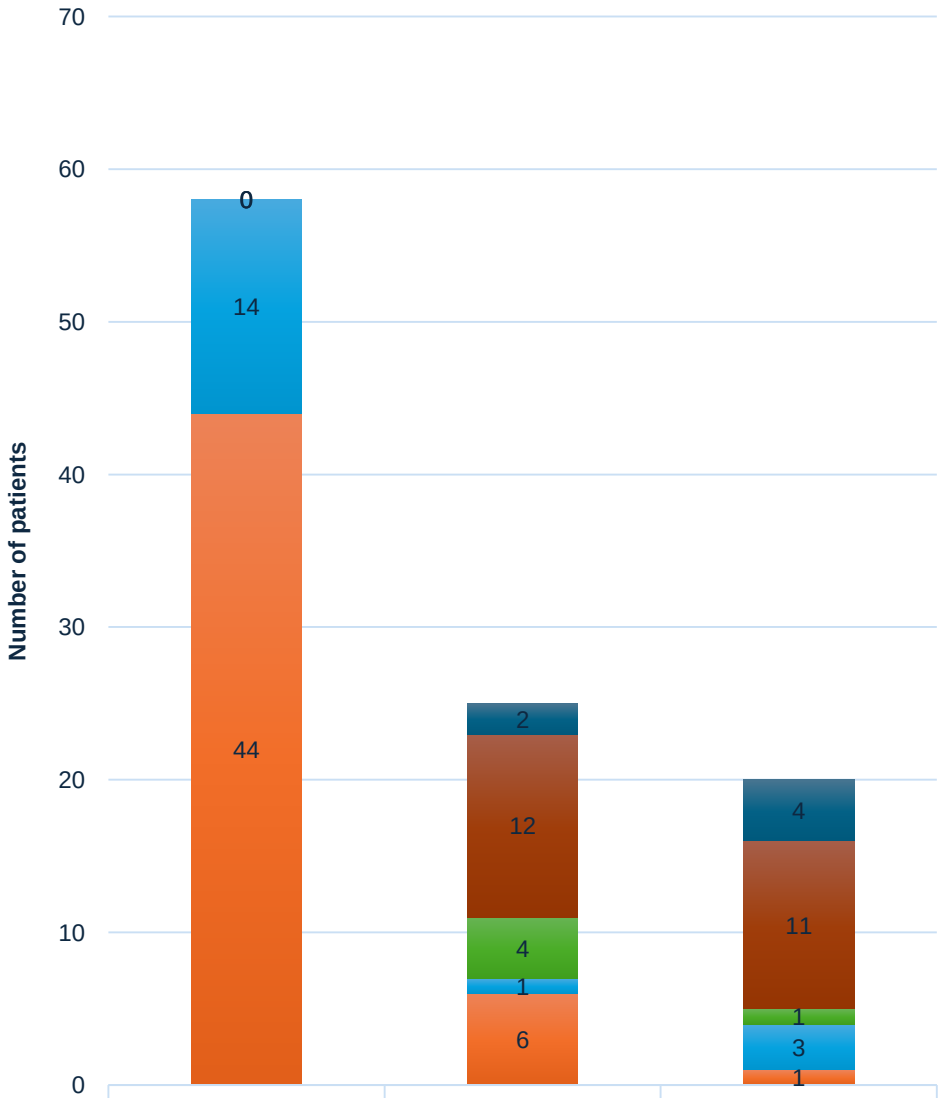
	MES 0	MES 1	MES 2	MES 3
NHI 4	2	0	2	2
NHI 3	7	10	4	2
NHI 2	4	1	0	0
NHI 1	12	5	1	0
NHI 0	41	9	1	0

Mayo endoscopic score

Table 18: Distribution and Correlation between LCI and Nancy Histological Index (n=103)						
	LCI A	LCI B	LCI C	Total	Spearman's rho	p-value
NHI 0	44	6	1	51	0.737	<0.001
NHI 1	14	1	3	18		
NHI 2	0	4	1	5		
NHI 3	0	12	11	23		
NHI 4	0	2	4	6		
Total	58	25	20	103		

Table-18 presents the distribution of NHI among LCI subgroups. The majority of patients (44/58) who have preserved vascular pattern and no mucosal redness, that is LCI A that signifies normal mucosa as per linked color imaging had histological remission and 14/58 had NHI-1 which signifies histological disease activity but only chronic inflammatory infiltrate with no acute inflammatory infiltrate. However, out of twenty five patients with LCI-B (mucosal redness with preserved vascular pattern) only six were in histological remission that is NHI-0 and 19/25 patients had histologically active disease (NHI-1 in 1/25, NHI-2 in 4/25, NHI-3 in 12/25 and NHI-4 in 2/25). Only one patient out of 20 had histological remission in LCI-C (Mucosal redness and obliterated vascular pattern) and 19/20 had histologically active disease (NHI-1 in 3/20, NHI-2 in 1/20, NHI-3 in 11/20, NHI-4 in 4/20). The data reveals a strong correlation between LCI and NHI (spearman’s rho - 0.737, p-value < 0.001). The total distribution of LCI and NHI values is shown in Figure-13. These findings suggest that LCI is a useful predictor of histological disease activity in patients with ulcerative colitis.

Figure 13: Distribution of NHI in LCI in Study Patients (n=103)



	LCI A	LCI B	LCI C
NHI 4	0	2	4
NHI 3	0	12	11
NHI 2	0	4	1
NHI 1	14	1	3
NHI 0	44	6	1

Nancy histological index

Table 19: MeanLCI Index among LCI subgroups in Study Patients (n=103)		
LCI	Mean LCI Index	p-value
LCI A	15.2	< 0.001
LCI B	39.8	
LCI C	47.5	

The LCI index was calculated in all 103 study patients (as described in material and methods) and distribution of LCI index among LCI subgroups is presented in Table-19. The mean LCI index values differed significantly across the subgroups (p-value < 0.001), with LCI-A having the lowest mean value (15.2), followed by LCI-B with a mean value of 39.8, and LCI-C having the highest mean value (47.5). The same is illustrated in Figure-14, a line diagram showing mean LCI index values for each LCI subgroups showing upward trend in LCI index values across subgroups suggests a correlation between LCI index and endoscopic LCI classification.

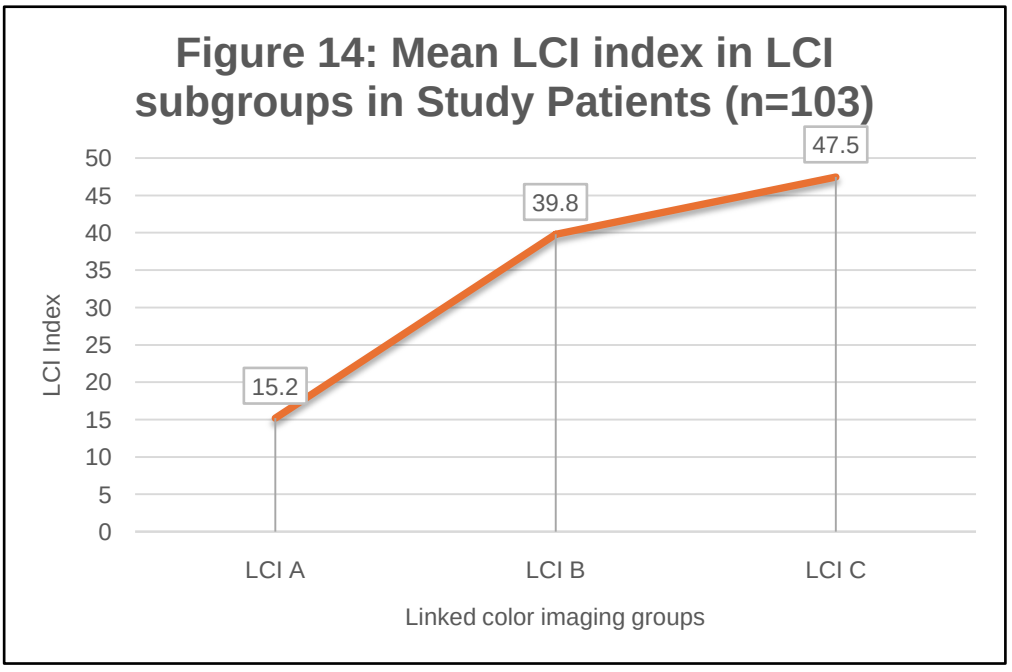


Table 20: Mean LCI Index among NHI subgroups in Study Patients (n=103)			
NHI	Mean LCI Index	Spearman's rho	p-value
NHI 0	18.6	0.663	< 0.001
NHI 1	20.4		
NHI 2	39.2		
NHI 3	44.9		
NHI 3	47.3		

The table-20 shows the mean LCI index values for each NHI subgroup, as well as the Spearman's rho correlation coefficient. The results indicate a strong positive correlation (Spearman's rho=0.663, p-value<0.001) between LCI index and NHI, suggesting that higher LCI index values are associated with higher NHI score. The mean LCI index value is lowest in NHI-0 (18.8), increases with increasing NHI scores, in NHI-1 (20.4), in NHI-2 (39.2), in NHI-3 (44.9) and in NHI-4 (47.3). The line diagram in Figure-15 depict a strong positive correlation between LCI index and NHI, with higher NHI scores associated with higher LCI index values. This correlation is visually represented by the upward-sloping line, highlighting the strong relationship between LCI index and NHI. This correlation supports the use of LCI index as a marker for disease severity in patients with ulcerative colitis.

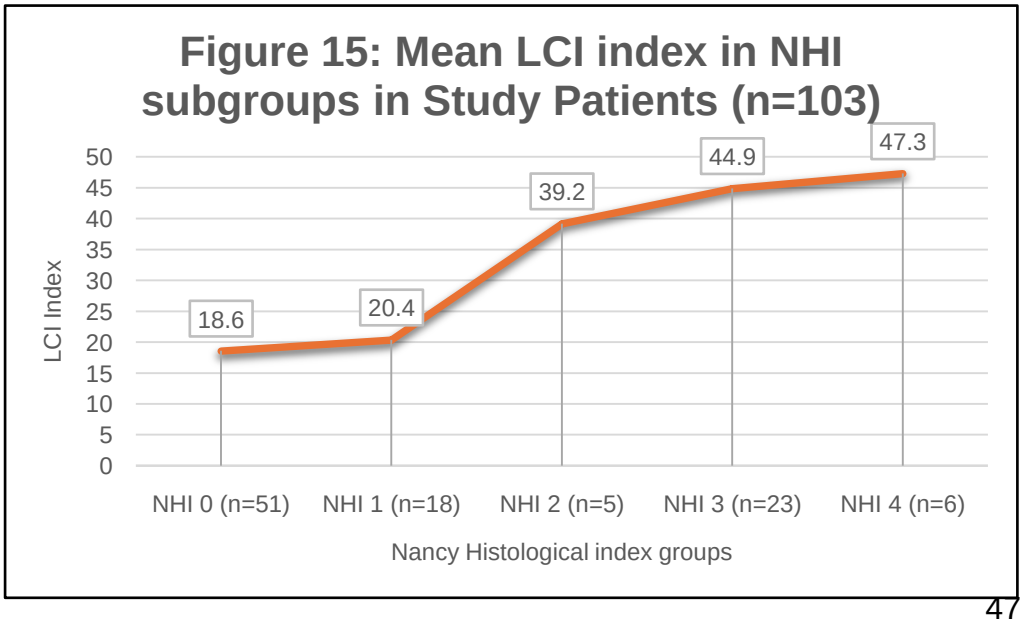


Table 21: Correlation of MES and LCI with NHI		
Parameter	Spearman's rho correlation coefficient	p-value
MES - NHI	O.449	<0.001
LCI - NHI	0.737	

As shown in Table-21 and Figure-16 & 17, the correlation between nancy histological index (NHI) and two endoscopic imaging modalities: white light endoscopy and linked color imaging. The curves represent the Spearman’s rho correlation coefficients, with a moderate correlation observed between MES and NHI (0.449, p-value < 0.001) and a strong correlation between LCI and NHI (0.737, p-value < 0.001). The steeper slope of the LCI curve indicates a more robust relationship with histological disease activity, suggesting that LCI is more accurate predictor of histological disease activity in patients with ulcerative colitis.

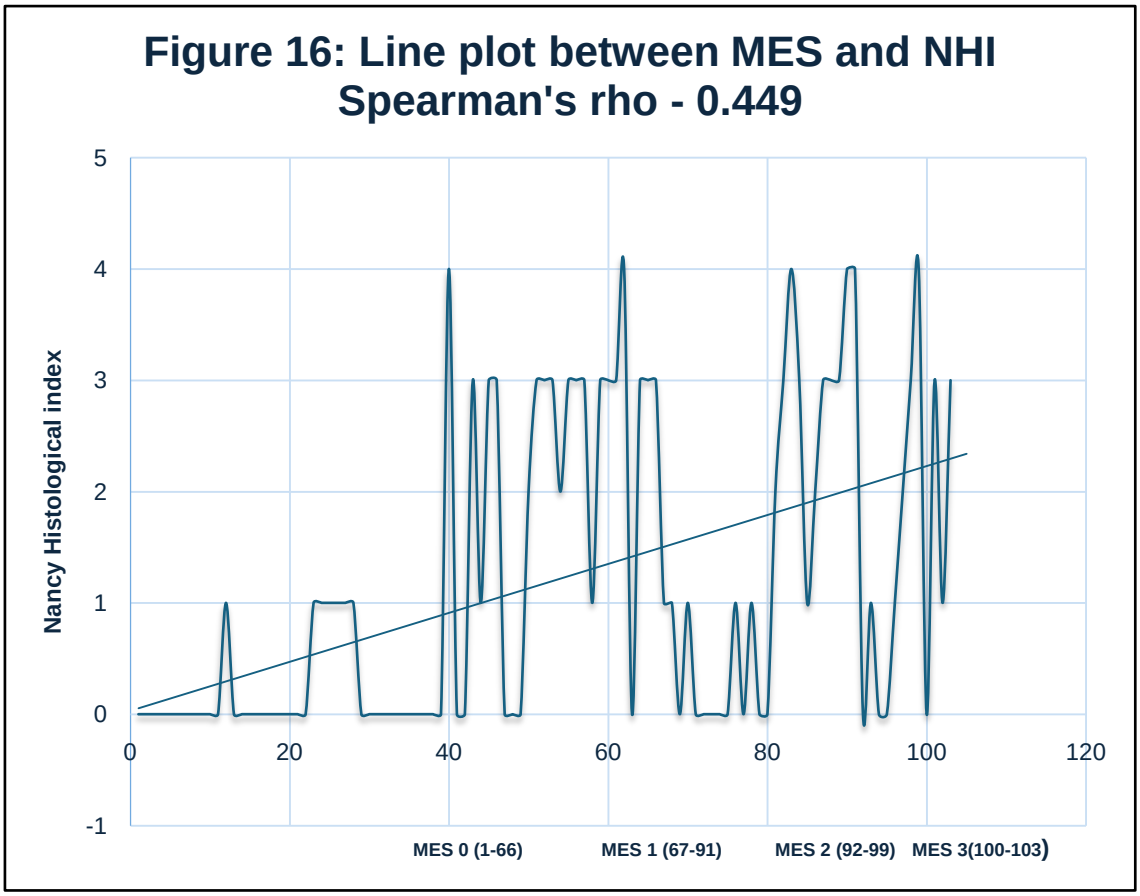


Figure 16: Line plot between MES and NHI
Spearman's rho - 0.449
Nancy Histological index
5
4
3
2
1
0
-1
0
20
40
60
80
100
120
MES 0 (1-66)
MES 1 (67-91)
MES 2 (92-99)
MES 3(100-103)

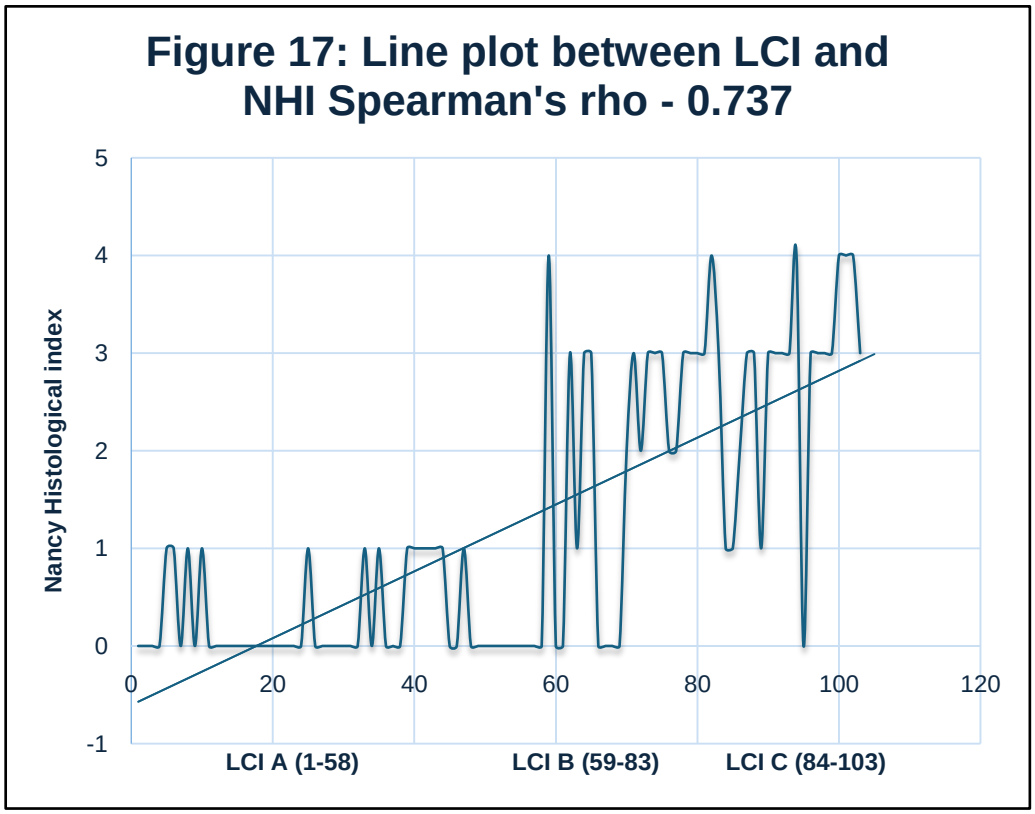


Figure 17: Line plot between LCI and NHI Spearman's rho - 0.737
Nancy Histological index
5
4
3
2
1
0
-1
0
20
40
60
80
100
120
LCI A (1-58)
LCI B (59-83)
LCI C (84-103)

Table 22: Mean Fecal Calprotectin among LCI subgroups (n=103)		
LCI	Mean Fecal Calprotectin (mcg/gm)	p-value
LCI A (n=58)	49.6	0.036
LCI B (n=25)	102.1	
LCI C (n=20)	185.9	

The mean fecal calprotectin (FC) levels among the LCI subgroups are presented in Table-22, which shows a significant increase in FC levels across the LCI subgroups, with LCI A (n=58) having a mean FC level of 49.6 mcg/gm, LCI B (n=25) having a mean FC level of 102.1 mcg/gm, and LCI C (n=20) having a mean FC level of 185.9 mcg/gm. This gradual increase in FC levels across the LCI subgroups is also illustrated in Figure-18, which shows a clear gradient of increasing FC levels as LCI severity progresses from LCI A to LCI C, reinforcing the finding that FC levels increase with increasing LCI severity, suggesting a potential role for FC as a non-invasive marker for disease activity in ulcerative colitis.

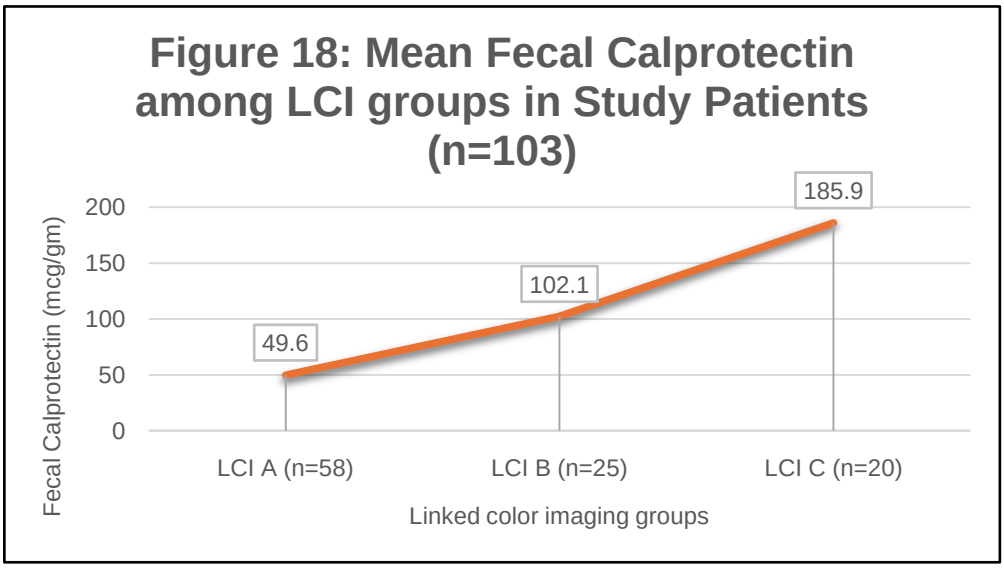


Table 23: Mean Fecal Calprotectin among MES subgroups (n=103)		
MES	Mean Fecal Calprotectin (mcg/gm)	p-value
MES 0 (n=66)	65.2	0.004
MES 1 (n=25)	60.2	
MES 2 (n=8)	328.8	
MES 3 (n=4)	177.5	

The mean fecal calprotectin (FC) levels among the MES groups are presented in Table 23. The results show a significant increase in FC levels across the MES groups, with MES 0 (n=66) having a mean FC level of 65.2 mcg/gm, MES 1 (n=25) having a mean FC level of 60.2 mcg/gm, MES 2 (n=8) having a mean FC level of 328.8 mcg/gm, and MES 3 (n=4) having a mean FC level of 177.5 mcg/gm. It can be seen from data that mean fecal calprotectin is higher in MES-2 compared to MES-3 as one patient with MES-2 had fecal calprotectin of 2000mcg/gm, otherwise there is a gradual increase in mean FC levels across the MES subgroups suggesting a positive correlation between FC level and MES severity, indicating that FC may be a useful marker for disease activity in patients with ulcerative colitis.This positive correlation is also illustrated in Figure 19.

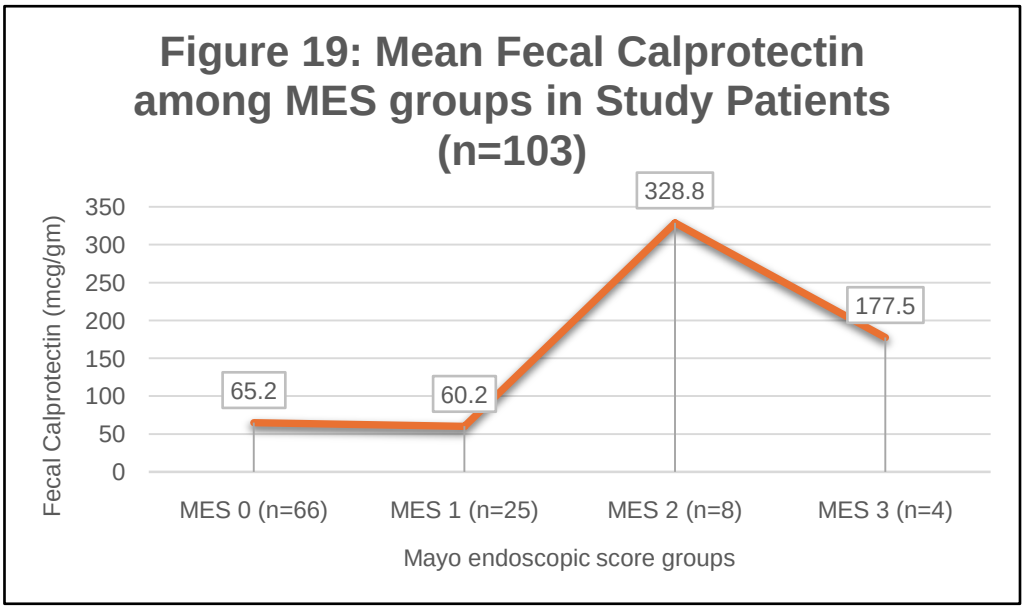
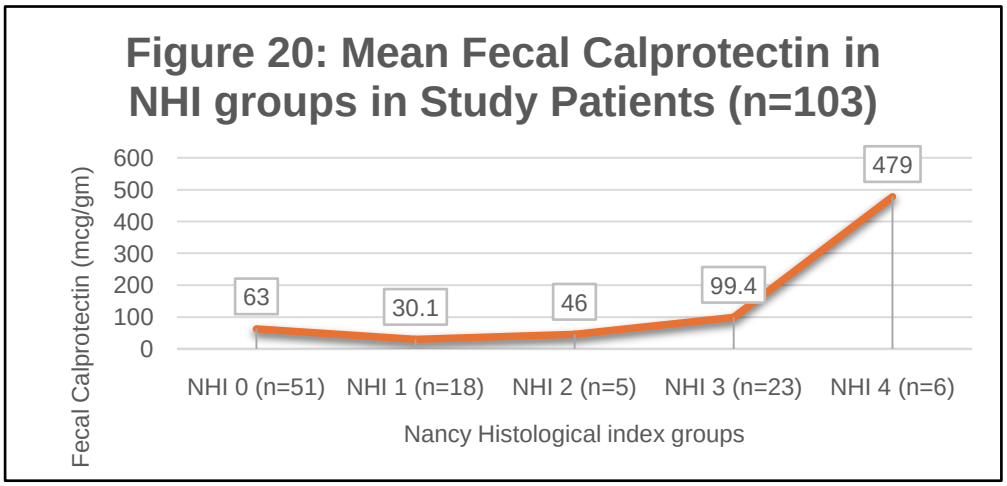
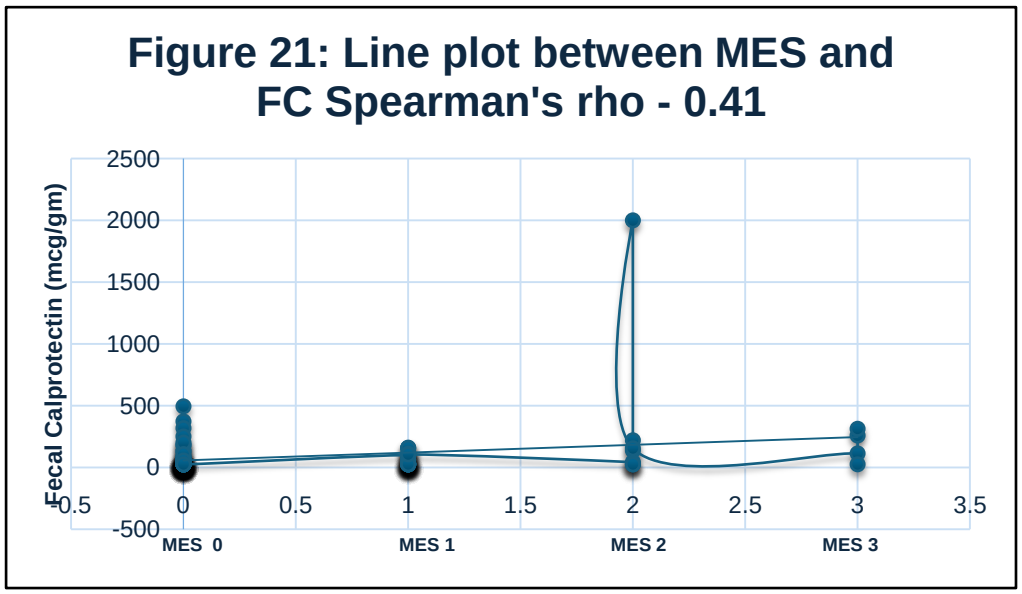


Table 24: Mean Fecal Calprotectin in NHI subgroups (n=103)		
NHI	Mean Fecal Calprotectin (mcg/gm)	p-value
NHI 0 (n=51)	63	0.001
NHI 1 (n=18)	30.1	
NHI 2 (n=5)	46	
NHI 3 (n=23)	99.4	
NHI 4 (n=6)	479	

The mean fecal calprotectin (FC) levels among the NHI groups are presented in Table-24. The results show that patients having NHI 0 (n=51) having a mean FC level of 63 mcg/gm, NHI 1 (n=18) having a mean FC level of 30.1 mcg/gm, NHI 2 (n=5) having a mean FC level of 46 mcg/gm, NHI 3 (n=23) having a mean FC level of 99.4 mcg/gm, and NHI 4 (n=6) having a mean FC level of 479 mcg/gm (p-value=0.001).This is also illustrated in Figure-20, which shows a marked increase in FC levels as NHI severity progresses from NHI 0 to NHI 4, highlighting the potential utility of FC as a non-invasive marker for disease activity in ulcerative colitis patients.





Figures 21 and 22 illustrate the correlations between MES, LCI, and FC levels. While MES and FC show a moderate positive correlation (Spearman's rho = 0.41) in Figure 22, LCI and FC exhibit a significantly stronger positive correlation (Spearman's rho = 0.64) in Figure 23. This suggests that FC levels correlate better with LCI compared to MES (p-value <0.001).

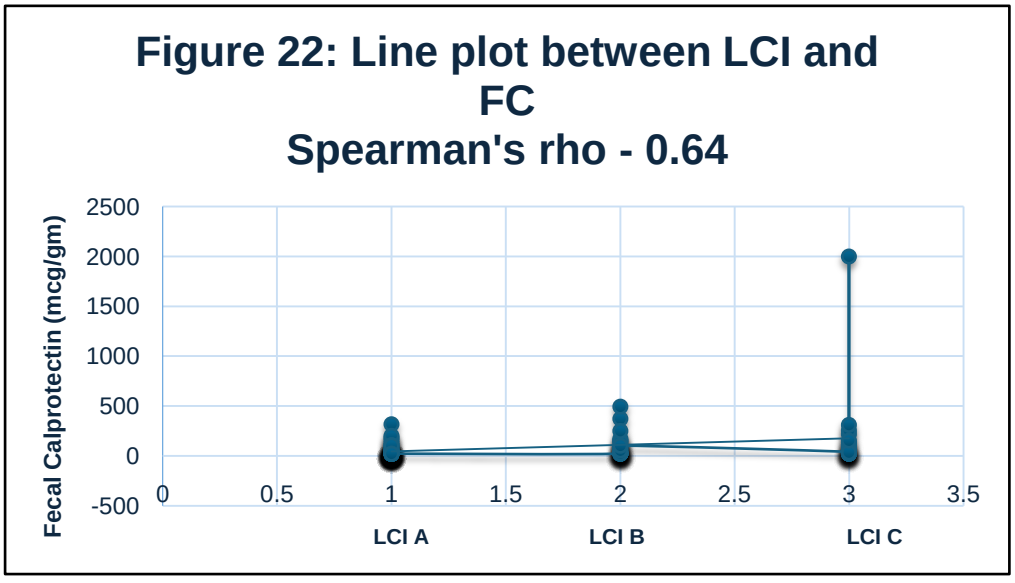


Table 25: Comparison of power to predict histological remission (NHI 0) between LCI A and MES 0. (Confidence interval 95%)		
Statistical parameter	MES 0	LCI A
Sensitivity (%)	80.3	86.2
Specificity (%)	51.9	73.0
Positive likelihood	1.67	3.2
Negative likelihood	0.38	0.19
Positive predictive value (%)	62.1	75.8
Negative predictive value (%)	72.9	84.4
Accuracy (%)	66.0	79.6

As highlighted in Table-25 and Figure-23, the statistical analysis showed that the linked color imaging can best predict the histological remission (i.e, NHI-0) with AUC 0.815 (CI 0.729-0.900) , followed by LCI index having AUC of 0.806 (CI 0.721-0.891) and lastly MES also predicts with AUC 0.678 (CI 0.574-0.782) with significant p-value < 0.001 (Figure-23).

Data has also shown that LCI A can predict histological remission (NHI-0) with sensitivity of 86.27% and specificity of 73.08% with positive likelihood ratio of 3.2 and positive predictive value of 75.86% and negative predictive value of 84.44% (confidence interval 95%) with higher accuracy when compared to MES-0 (LCI-A 79.6% vs MES-0 66%), which can predict histology remission (NHI-0) with sensitivity of 80.39% and specificity of 51.92% with positive likelihood ratio of 1.67 and positive predictive value of 62.12% and negative predictive value of 72.97% (confidence interval 95%).

Fig-23 :Comparative ROC Curve Analysis to predict histological remission: LCI, LCI Index, and MES. p-value<0.001.

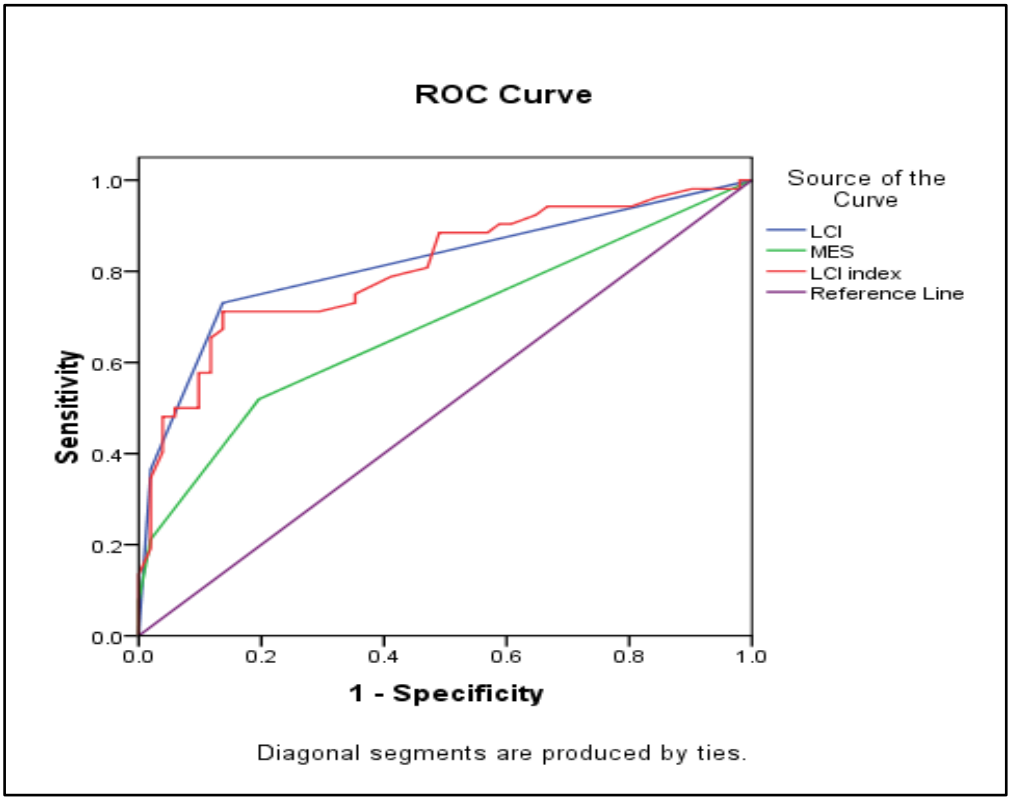


Table 26: Agreement between MES and NHI scores – Kappa Analysis					
	NHI 0	NHI > 0	Total	Kappa	p-value
MES 0	41	25	66	0.322	0.001
MES >0	10	27	37		
Total	51	52	103		

Table 27: Agreement between LCI and NHI scores – Kappa Analysis					
	NHI 0	NHI > 0	Total	Kappa	p-value
LCI A	44	14	58	0.539	0.001
LCI B&C	7	38	45		
Total	51	52	103		

Table 28 : Kappa Statistics and Z-Scores for Agreement between LCI/MES and NHI Scores			
	Kappa value	Z-score	p-value
LCI A - NHI 0	0.539	2.23	<0.05
MES 0 - NHI 0	0.322		

Table 26, 27 & 28 highlighted the agreement of MES 0 and LCI A in predicting histological remission (NHI 0). A comprehensive statistical analysis was conducted to compare the performance of MES and LCI in predicting histological remission. The kappa values for mayo endoscopic score and nancy histological index, and linked color imaging and nancy histological index were calculated to be 0.322 (SE = 0.075) and 0.539 (SE = 0.081), respectively. The z-score for the difference between the two kappa values was calculated to be 2.23 ($p < 0.05$), indicating a statistically significant difference. This result suggests that LCI A has a significantly higher agreement with histological remission (NHI 0) compared to MES 0. The kappa value for LCI (0.539) indicates a moderate to substantial agreement, whereas the kappa value for MES (0.322) indicates a fair agreement. Therefore, LCI A is a better predictor of histological remission than MES. The findings of this study have important implications for the diagnosis and treatment of ulcerative colitis. The use of LCI A as a predictive tool may lead to improved patient outcomes, more accurate diagnosis, and potentially more effective treatment strategies.

DISCUSSION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease that causes relapsing and remitting mucosal inflammation, most commonly affecting the colon and rectum.[1] One of the primary goals in UC management is to achieve and maintain mucosal healing (MH), which is associated with improved clinical outcomes, including sustained remission and reduced rates of hospitalization and colectomy.[13] Conventional assessments of MH have relied on white light endoscopy (WLE) and histological examination through biopsy. However, WLE has limitations in detecting subtle mucosal changes, and biopsies can be invasive and resource-intensive. Linked color Imaging (LCI) has emerged as a promising endoscopic technology that enhances mucosal visualization by improving color contrast, potentially offering a more accurate and less invasive method for assessing inflammation.[38] Previous clinical studies have defined mucosal healing (MH) as a MES of 0 or 1. However, a closer examination of the long-term outcomes reveals a significant disparity between patients with a MES of 0 and those with a sub score of 1. Specifically, studies have shown that patients with a sub score of 0 have markedly better long-term outcomes compared to those with a sub score of 1. For instance, the ACT-1 and ACT-2 clinical studies reported a remission rate of 73% after 54 weeks in patients with a sub score of 0, compared to 47% in those with a sub score of 1.[39,89] Similarly, Barreiro-de Acosta et al. found that patients with a sub score of 0 had a relapse rate of 9.4% during the first 6 months, whereas those with a sub score of 1 had a relapse rate of 36.6%.[18] Furthermore, Yokoyama et al. reported 5-year relapse-free rates of 78% and 40% for patients with sub scores of 0 and 1, respectively.[90] Nakaral et al. also found that patients with a sub score of 1 had a significantly higher long-term risk of clinical relapse compared to those with a sub score of 0.[91] These findings suggest that a Mayo endoscopic sub score of 1 is not an appropriate indicator of mucosal remission due to the high relapse rate. Moreover, even patients with a sub score of 0 experienced some relapse, highlighting

the need for new endoscopic criteria to predict prognosis and understand the pathophysiology of UC accurately.

This study investigates the clinical utility of LCI, a novel endoscopic enhancement system, in patients with UC who have achieved symptomatic remission. It compares the effectiveness of LCI to WLE in assessing mucosal healing and histological activity in these patients. Despite symptomatic remission, some UC patients may still have underlying mucosal inflammation, which can predict future relapse. Accurate assessment of mucosal healing is crucial for personalized management and optimal patient outcomes. Recent advancements in endoscopic technology, such as LCI, provide new opportunities to enhance mucosal visualization and objectively assess disease activity.[38,80-86] This study aims to explore the correlation between LCI-enhanced mucosal redness, white light imaging, and histology, as well as evaluate LCI potential to predict mucosal healing in patients with UC.

Our study offers significant insights into the evaluation of disease activity in patients with UC, focusing on the correlation between endoscopic imaging modalities (white light endoscopy, linked color imaging) and histological activity. The demographic distribution of our study patients reveals that UC is more common in younger age groups, with the majority aged between 31 and 40 years, while the mean age at diagnosis was 32.5 years, consistent with other study from India.[92] The gender distribution showed a higher prevalence among females (62.1%), which in contrast is more compared with western as well as Indian data which indicates gender distribution in UC is either equal or associated with male preponderance,[92-94] this difference cannot be explained as present study is hospital based which may not be representative of whole population. The mean disease duration of 7.3 years, with a diagnostic delay of approximately 8 months. The extent of disease in our cohort was primarily limited to left-sided colitis (68.9%), followed by proctitis (19.4%) and pan-colitis (11.7%). This distribution suggests that limited colonic involvement is more common in our

patient population, in contrast to data from other studies from India, Asia and across globe.[92,95-97]The hospital-based design may limit its generalizability to the entire population, making it difficult to attribute the observed difference to a specific factor.

The mayo endoscopic score is commonly used to assess mucosal healing in UC patients. In our study, 88.4% (91/103) of patients achieved endoscopic remission by WLE (MES-0 in 66/103 and MES-1 in 25/103), indicating that a significant portion of the cohort achieved visible mucosal healing. However, only 49.5% (51/103) of patients were found to be in histological remission. Patients classified as MES-0 had a high rate of histological remission (NHI-0, 41/66), but a significant number still had chronic moderate to severe histological inflammation (NHI-1 in 12/66), mild active disease (NHI-2 in 4/66), moderately active disease (NHI-3 in 7/66) and severely active disease (NHI-4 in 2/66). Notably, MES-1 was associated with considerable histological activity, only 36% (9/25) patients were in histological remission, 64% (16/25) patients had histologically active disease, underscoring the limitations of relying solely on white light endoscopy to evaluate true mucosal healing. we found a moderate correlation between MES and histological activity (Spearman's rho 0.449, $p < 0.001$), with many patients in MES-0 and MES-1 groups still having histologically active disease. Our results reflect findings from previous studies suggesting that MES alone may not be a reliable predictor of histological remission, moreover similar discrepancies between endoscopic and histologic findings have been reported by others.[98-100]

LCI, a novel endoscopic technique, showed a stronger correlation with histological findings compared to MES. In our study, 58 patients were classified as LCI-A (normal mucosa), 25 as LCI-B (mucosal redness with preserved vascular pattern), and 20 as LCI-C (mucosal redness with obliterated vascular pattern). Linked color imaging has divided MES-0 into LCI A (50/66), LCI B (16/66) and none had LCI C. LCI has further divided MES-1 into LCI A (8/25), LCI B (9/25) and LCI C (8/25). All patients with MES-2 and MES-3 had LCI C (12/12). The data also reveals a strong correlation between LCI and MES (spearman's

rho=0.673, p-value<0.001). The majority of LCI A patients had histological remission (NHI-0 in 44/58) while 14/58 had NHI-1 which signifies histological disease activity but only chronic inflammatory infiltrate with no acute inflammatory infiltrate. However, out of twenty five patients with LCI-B only six were in histological remission and 19/25 patients had histologically active disease (NHI-1 in 1/25, NHI-2 in 4/25, NHI-3 in 12/25 and NHI-4 in 2/25). Only one patient out of 20 had histological remission in LCI-C and 19/20 had histologically active disease (NHI-1 in 3/20, NHI-2 in 1/20, NHI-3 in 11/20, NHI-4 in 4/20). The data reveals a very strong correlation between LCI and NHI (spearman's rho – 0.737, p-value < 0.001). These findings suggest that LCI is a useful predictor of histological disease activity in patients with ulcerative colitis and can detect subtle changes in mucosal inflammation that may not be evident on standard white light endoscopy. LCI shows a better performance to predict histological remission (AUROC for LCI was 0.815 and for MES was 0.678, p-value < 0.001). Also, LCI A showed superior performance to MES 0 in predicting histological remission(NHI 0), with a moderate to substantial agreement (kappa value=0.539 for LCI with NHI and Kappa value=0.322 for MES and NHI, z-score=2.23, p<0.05).

LCI index was calculated in all study patients which quantify the mucosal redness. The mean LCI index values differed significantly across the endoscopic LCI subgroups (p-value < 0.001), with LCI-A having the lowest mean value (15.2), followed by LCI-B with a mean value of 39.8, and LCI-C having the highest mean value (47.5). The results indicate a strong positive correlation (Spearman's rho=0.663, p-value<0.001) between LCI index and NHI, suggesting that higher LCI index values are associated with higher NHI score. The mean LCI index value are lowest in NHI-0 (18.8), increases with increasing NHI scores, in NHI-1 (20.4), in NHI-2 (39.2), in NHI-3 (44.9) and in NHI-4 (47.3) (p-value<0.001).

Fecal calprotectin (FC) levels were significantly associated with both endoscopic and histological disease severity in our study. The mean FC levels increased progressively across LCI subgroups, from 49.6

mcg/g in LCI-A to 185.9 mcg/g in LCI-C, showing a significant correlation with both LCI (Spearman's rho 0.64) and histological activity (Spearman's rho 0.663). This strong correlation supports the utility of FC as a non-invasive biomarker for mucosal inflammation. Interestingly, FC levels correlated better with LCI compared to MES, reinforcing the hypothesis that LCI is a more sensitive indicator of active mucosal inflammation.

The role of LCI in evaluating mucosal inflammation in UC has been explored in several recent studies, which support our findings. The study by Uchiyama et al. (2017) demonstrated that LCI effectively assessed mucosal inflammation and predicted relapse in 52 UC patients in remission. LCI was able to subdivide MES grades more precisely, with 46.4% of MES-0 areas showing redness (41.8% LCI-B and 4.6% LCI-C), and 60.5% of MES-1 areas classified as LCI-C. These classifications strongly correlated with histopathological findings, revealing higher Matts grades in LCI-B and LCI-C areas. During follow-up, 64.3% of relapsed patients were classified as LCI-C, while none in LCI-A relapsed ($p = 0.0055$).[38] Our study aligns with these findings, showing a strong correlation between LCI and histological activity (Spearman's rho = 0.737, $p < 0.001$), where LCI-A patients had a 75.9% (44/58) histological remission rate, and LCI-C exhibited histological disease activity in 95% (19/20) of patients. We also found that LCI effectively subdivided MES, particularly in MES-0 and MES-1 patients, underscoring LCI sensitivity as a predictor of mucosal inflammation and relapse in UC patients

Kanmura et al. (2019) evaluated LCI for assessing colonic mucosal inflammation in UC, finding significantly higher LCI-a and LCI-b values in patients with active inflammation ($p < 0.01$), while conventional white-light imaging (WLI) showed no significant differences. LCI-a correlated with histological healing scores, and the difference in color values (ΔE) was greater with LCI ($\Delta E = 7.1$) than WLI ($\Delta E = 3.1$), suggesting LCI superior sensitivity.[81] Our study aligns with these findings, despite 88.4% achieving MES-0 or MES-1, only 49.5% were in histological remission. LCI demonstrated a strong correlation with

histological findings (Spearman's rho = 0.737, $p < 0.001$) with LCI-A patients showing a high histological remission rate, while LCI-C patients exhibited severe inflammation. These results underscore LCI utility as a sensitive predictor of mucosal inflammation, capable of detecting subtle changes not evident with WLI.

Takagi et al. (2021) demonstrated that LCI predicted relapse in UC more effectively than the MES. Over 48 months, none of the LCI-A patients relapsed, while 47.1% of LCI-B patients did ($p = 0.018$), showing LCI superior sensitivity. LCI further subdivided MES-0 into LCI-A (34.6%) and LCI-B (65.4%), detecting subtle mucosal changes that MES missed.[82] Our study aligns with these findings, as LCI subdivided MES-0 into LCI-A (50/66) and LCI-B (16/66), and further divided MES-1 into LCI-A (8/25), LCI-B (9/25), and LCI-C (8/25). LCI also showed a stronger correlation with histological activity (Spearman's rho = 0.737, $p < 0.001$) compared to MES (Spearman's rho = 0.449, $p < 0.0001$), with LCI-A predicting histological remission more accurately. Both studies confirm LCI superior ability to assess mucosal healing and predict disease activity.

Matsumoto et al. (2020) demonstrated that LCI more accurately assessed endoscopic activity and predicted relapse in UC patients compared to WLI. In a study of 72 UC patients, they found that LCI was able to detect subtle mucosal inflammation missed by WLI, with a significant correlation between LCI findings and histopathological inflammation (Geboes score, GS). Specifically, GS of 0 or 1 was present in 89% of WLI-/LCI- sites, while 42% of WLI-/LCI+ sites had a GS of 2 or 3, highlighting LCI sensitivity in detecting mild inflammation. During follow-up, patients in the WLI-/LCI- group had no relapses, while 10 patients in the WLI+/LCI+ group and four in the WLI-/LCI+ group relapsed. Non-relapse rates were significantly correlated with LCI classification but not with MES.[84] Our study mirrors these findings, with LCI subdividing MES-0 into LCI-A and LCI-B, and MES-1 into LCI-A, LCI-B, and LCI-C. LCI demonstrated a stronger correlation with histological activity (Spearman's rho = 0.737, $p < 0.001$) compared to MES (rho = 0.449, $p < 0.0001$). Furthermore, LCI more accurately

predicted histological remission, with a moderate to substantial agreement with histology (kappa = 0.539) compared to MES (kappa = 0.322). These findings underscore the utility of LCI in detecting mucosal changes that predict disease relapse and histological activity more effectively than WLI.

The utility of LCI in UC management is further supported by recent studies, such as that of Saito D. et al. (2023), which evaluated the correlation between LCI and histopathological findings. In their study, conducted across multiple Japanese institutions, 92 UC patients in clinical remission (MES ≤1) were evaluated using a newly developed LCI index that included three key parameters: redness, area of inflammation (A), and lymphoid follicles (L), graded on scales of 0-2 or 0-3. Their findings indicated significant associations between histological healing and LCI index-R (P = 0.013) as well as LCI index-A (P = 0.0014), reinforcing the idea that LCI can predict histological outcomes with high accuracy. The histological healing rate was 84.0%, further highlighting the effectiveness of the LCI index in assessing mucosal inflammation in UC patients with MES ≤1 and clinical remission.[85] Our study showed that 88.4% of patients achieved endoscopic remission on WLI, however only 49.5% were in histological remission, indicating discrepancies between endoscopic and histological findings. We found a moderate correlation between MES and histological activity (Spearman's rho 0.449, $p < 0.0001$), suggesting MES may not reliably predict histological remission. In contrast, LCI showed a strong correlation with histological findings (Spearman's rho 0.737, $p < 0.001$). The LCI index indicated significant differences across histological subgroups (p-value < 0.001) and correlated positively with histological scores (Spearman's rho=0.663, $p < 0.001$).

Histological healing has become an increasingly important target in UC management, as persistent microscopic inflammation is associated with a higher risk of relapse, even in patients who achieve endoscopic remission. The study by Patel M. et al. (2022) demonstrated that LCI on the Fujifilm Eluxeo TM platform effectively predicts mucosal healing

and inflammation in UC patients, achieving an AUROC of 0.92, significantly higher than white light endoscopy (AUROC = 0.79). The a* value in LCI distinguished mucosal healing from active disease, showing significant differences (a* = 15.2±9.9 vs. a* = 37.2±10.3, p<0.001), with strong correlations to histological grading (r = 0.68) and fecal calprotectin levels (r = 0.53).[86] Our study aligns with these findings, revealing that LCI outperformed MES in predicting histological remission (AUROC for LCI: 0.815 vs. MES: 0.678, p<0.001), with LCI A showing superior performance to MES 0 in predicting histological remission (NHI 0), with a moderate to substantial agreement (kappa value=0.539 for LCI with NHI and Kappa value=0.322 for MES and NHI, z-score=2.23, p<0.05). These results suggest that LCI can provide a more accurate assessment of mucosal healing and could reduce the need for invasive biopsies. The mean FC levels increased progressively across LCI subgroups, from 49.6 mcg/g in LCI-A to 185.9 mcg/g in LCI-C, showing a significant correlation with both LCI (Spearman's rho 0.64, p-value <0.001) and histological activity (Spearman's rho 0.663, p-value <0.001), highlighting its role as a non-invasive biomarker for mucosal inflammation. Overall, our findings suggest that LCI is more sensitive indicators of mucosal healing than traditional assessments.

The findings of our study, combined with the evidence from previous research, suggest that LCI is a valuable tool for assessing mucosal healing in UC patients. By providing a more accurate and objective assessment of mucosal inflammation, LCI has the potential to improve clinical decision-making and guide treatment strategies. For instance, LCI could be used to identify patients who are at risk of relapse despite appearing to be in endoscopic remission based on WLE. These patients could benefit from closer monitoring and more aggressive treatment to prevent relapse and achieve sustained remission. Moreover, the ability of LCI to provide a quantitative measure of mucosal redness through the LCI index offers a standardized approach to assessing inflammation, reducing the variability associated with subjective endoscopic scoring systems such as the MES.

LIMITATIONS

Despite the promising results, our study has several limitations. First, the cross-sectional design limits our ability to evaluate the long-term predictive value of LCI for clinical relapse and response to treatment. Future longitudinal studies are needed to confirm the role of LCI in predicting long-term outcomes. Second, our study was conducted at a single centre, which may limit the generalizability of our findings to other populations or clinical settings. Additionally, while the LCI index offers a quantitative measure of mucosal inflammation, there is currently no standardized cut-off for clinical decision-making, and further research is needed to establish these thresholds.

SUMMARY

A total of 103 patients with ulcerative colitis (UC) were included in the study, following written informed consent. The study was conducted prospectively, incorporating patient history, clinical examination, and laboratory investigations, and the patients who were in symptomatic remission were included. All patients underwent colonoscopy/ sigmoidoscopy using high-definition endoscopy systems, with both white light imaging (WLI) and linked color imaging (LCI). LCI images were analyzed using Photoshop CS6 to calculate the a* value from the CIELAB color space, providing an objective redness index for inflammation. Biopsies were performed and graded using the Nancy Histological Index (NHI) to assess the degree of inflammation.

The majority of patients (28.8%) were aged between 31-40 years, with a female predominance of 62.1%.The mean disease duration in the cohort was 7.3 years, with an average diagnostic delay of 8 months. Left-sided colitis was the most common presentation, affecting 68.9% of the patients. The mean BMI was 23.2 kg/m2.The mean hemoglobin level was 12.3 gm/dl, while the mean fecal calprotectin (FC) level was 88.8 mcg/gm. Hypertension was present in 3.9% of patients, and diabetes was reported in 1.9% of the cohort. The majority of patients were non-alcoholic (98%) and non-smokers (99%). A family history of inflammatory bowel disease was reported by 2.9% of the patients. All patients received oral 5-ASA, while 35 were treated with tofacitinib, thiopurines was used in 26, four patients has undergone FMT and one was biologics (infliximab) experienced.

Based on the Partial Mayo Score (PMS), 88 of patients achieved a PMS of 0, while 15 had a PMS of 1.The majority of patients (n=66) had a MES of 0, followed by MES 1 in 25, MES 2 in 8, and MES 3 in 4 of patients. LCI A (no mucosal redness) was observed in 58 patients, LCI B (redness with preserved vascular pattern) in 25 patients, and LCI C (redness with obliterated vascular pattern) in 20 patients. Histological examination showed that 49.5% (51/103) of patients were in histological remission (NHI 0) and 51.5% (52/103) had some grade of

histological disease activity. Mean LCI index values increased progressively with histological severity, NHI 0 (18.6). NHI 1 (20.4), NHI 2 (39.2), NHI 3 (44.9) and NHI 4 (47.3). There was a strong correlation between LCI index values and NHI (Spearman's rho= 0.663, p-value < 0.001), indicating that higher LCI index values were associated with increased histological activity. A strong correlation was observed between LCI and NHI (Spearman's rho = 0.737, p-value < 0.001). A moderate correlation was found between MES and NHI (Spearman's rho=0.449, p-value < 0.001). LCI shows a better performance to predict histological remission (AUROC for LCI was 0.815 and for MES was 0.678, p-value < 0.001). Also, LCI A showed superior performance to MES 0 in predicting histological remission (NHI 0), with a moderate to substantial agreement (kappa value=0.539 for LCI with NHI and Kappa value=0.322 for MES and NHI, z-score=2.23, p<0.05).

CONCLUSION

In conclusion, our study demonstrates that LCI is a superior tool compared to WLE for assessing mucosal healing and predicting histological healing in UC patients. LCI provides a more accurate and objective assessment of mucosal inflammation, with strong correlations between LCI index values and histological severity. The findings of our study, along with the evidence from previous research, support the use of LCI as a better tool for disease activity, may obviate the need for mucosal biopsies and highlight its potential to improve the management of UC patients. Future studies should focus on validating these findings in larger, multi-center cohorts and exploring the role of LCI in predicting long-term outcomes.

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IMAGES

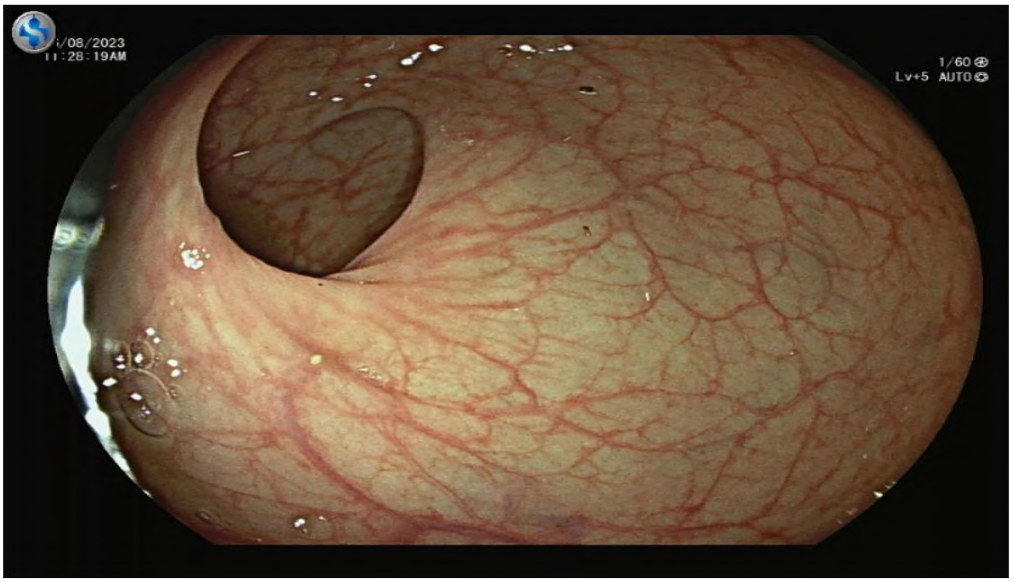

Image 1 – Colonoscopy image with white light showing normal mucosa with preserved vascular pattern corresponding to MES 0.

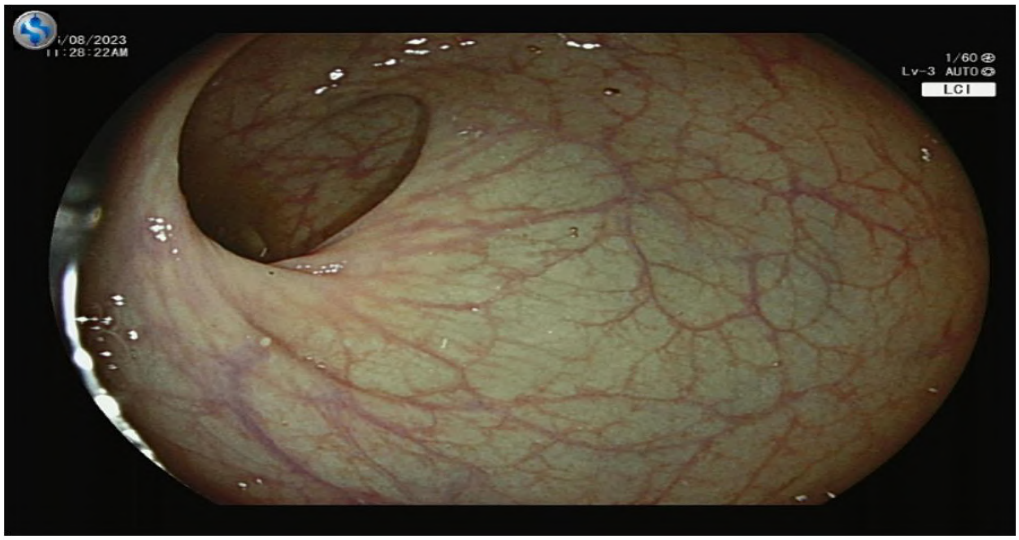

Image 2 – Colonoscopy image as shown in image 1, with linked color imaging showing no redness of mucosa with preserved vascular pattern corresponding to LCI A.

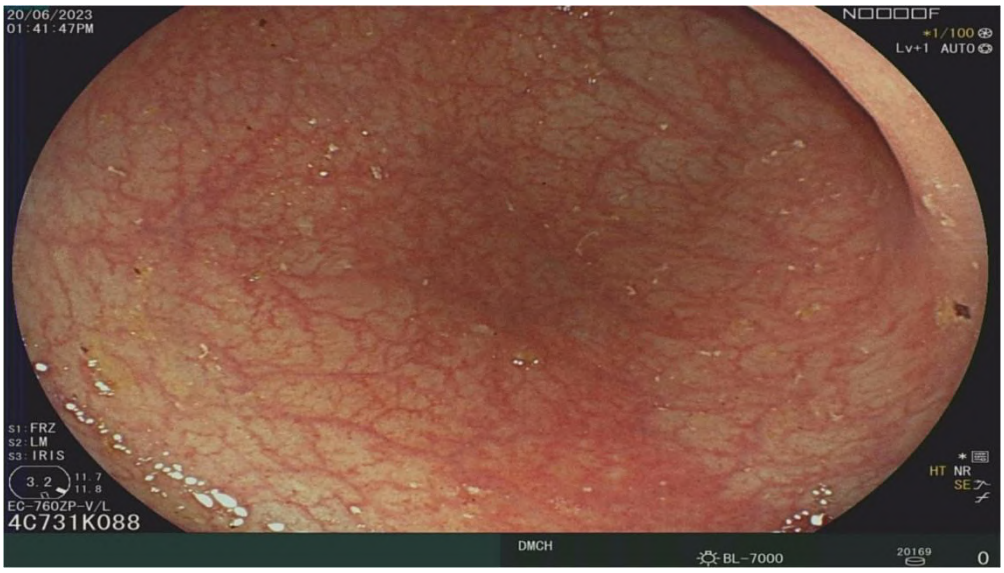

Image 3 - Colonoscopy image with white light showing preserved vascular pattern with patch of mucosal hyperemia corresponding to MES 1.

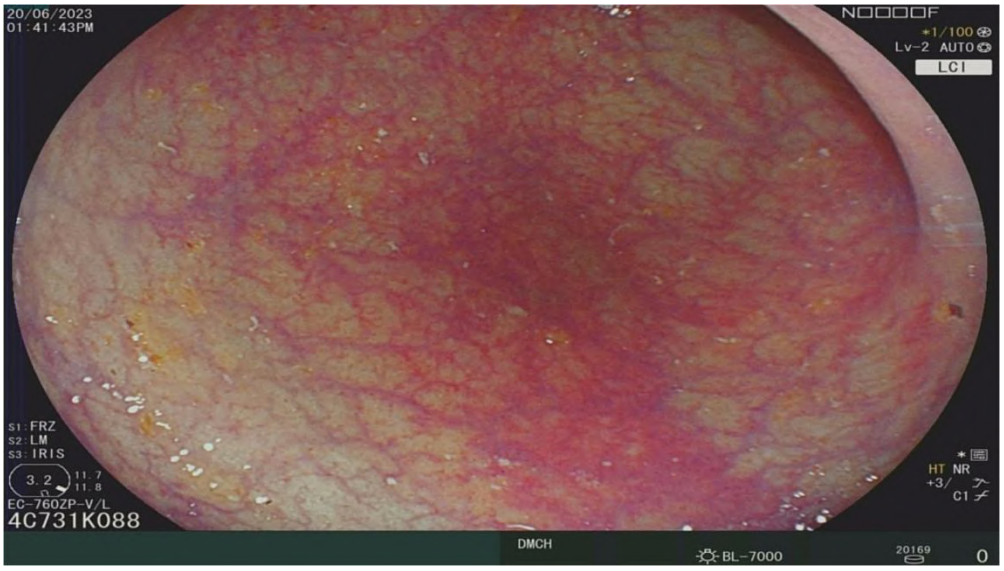

Image 4 - Colonoscopy image as shown in image3, with linked color imaging showing marked redness of mucosa with preserved vascular pattern corresponding to LCI B.

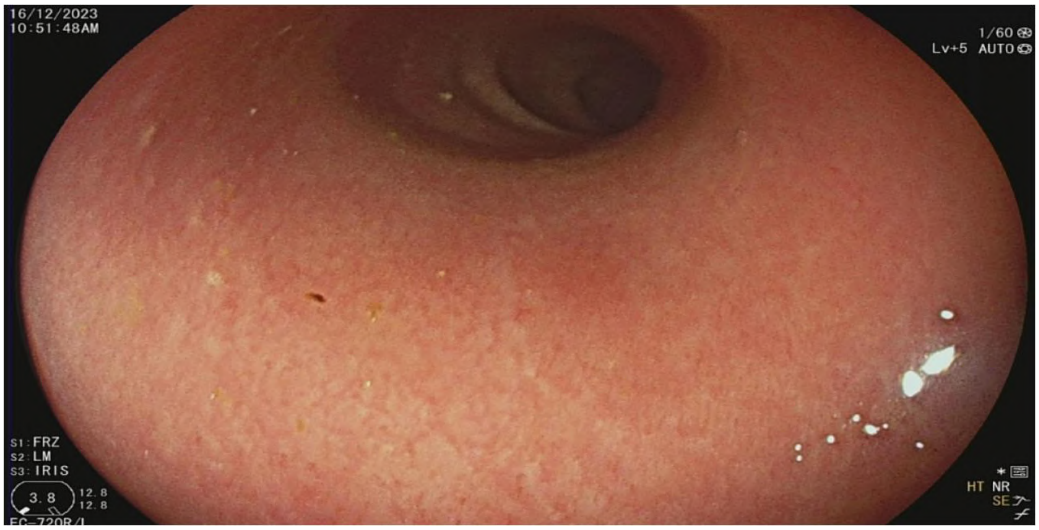

Image 5 - Colonoscopy image with white light showing decrease vascular pattern with mild mucosal edema however, no evidence of hyperemia, erosion, ulcers or bleeding corresponding to MES 1.

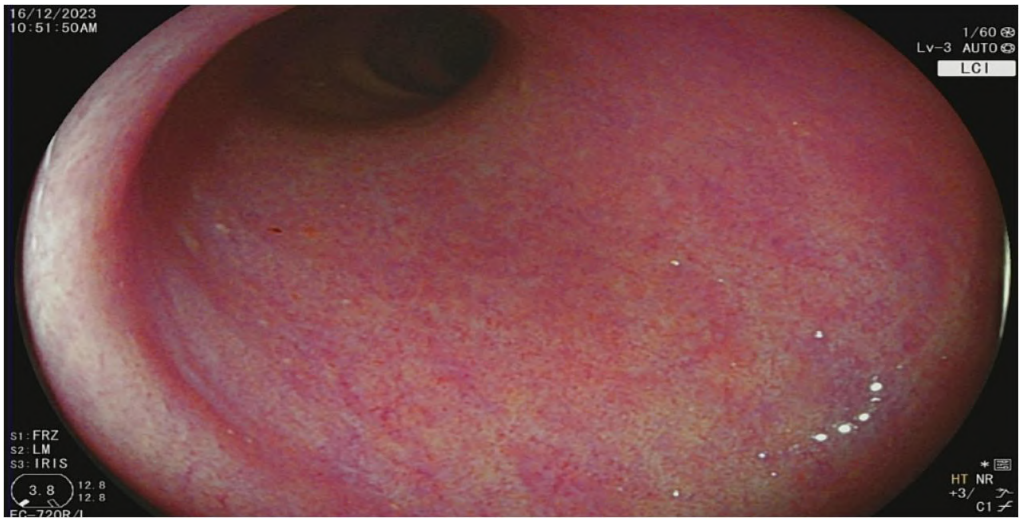

Image 6 - Colonoscopy image as shown in image 5, with linked color imaging showing marked redness of mucosa with obliterated vascular pattern corresponding to LCI C.

KEY TO MASTERCHART

Serial no.	Variable	Represent
1	S. No	Serial number of enrolled patients
2	MRD	Medical record department unique identification number
3	Initials	First alphabet of First and last name
4	Age	Age of enrolled patients in Years
5	Sex	Gender of enrolled patients M- Male, F-Female
6	Hypertension	0-Normotensive, 1-Hypertensive
7	Diabetes	0-Non diabetic, 1-Diabetic
8	Coronary artery disease	0-Absent, 1- Present
9	Hypothyroid	0-Not Hypothyroid, 1-Hypothyroid
10	Cerebrovascular disease	0-Absent, 1-Present
11	Alcohol use	0-Non alcoholic, 1-Alcoholic
12	Smoking	0-Non smoker, 1- Smoker
13	Age at onset of symptoms	Age when symptoms started (in years)
14	Age at diagnosis	Age when disease was diagnosed (in years)
15	Year of diagnosis	Calendar year when disease was diagnosed
16	Disease duration	Disease duration at the time of enrollment In years
17	Disease extent	Colonoscopic disease extent 1-Proctitis, 2-Left side colitis, 3-Pancolitis
18	Family History of IBD	0-No UC in other family members, 1-UC present in other family members
19	Height	Height of enrolled patients in Centimetres
20	Weight	Weight of enrolled patients in Kilograms

21	BMI	Body mass index (In Kg/$m^{2)}$
22	MUAC	Mid upper arm circumference in Centimetres
23	Hand grip strength	Hand grip strength measured with dynanometer in Kilograms
24	Hemoglobin	Hemoglobin of enrolled patients in gram/dl
25	PCV	Packed cell volume (in %)
26	MCV	Mean corpuscular volume (in femtolitre)
27	TLC	Total leukocyte count in (1000/microltr)
28	Platelets	Platelets of enrolled patients (in 1000/microltr)
29	ESR	Erythrocyte sedimentation rate (in mm1st hour)
30	CRP	C-reactive protein (in mg/litre)
31	FC	Fecal calprotectin (in microgram/gram of feces)
32	Albumin	Albumin of enrolled patients (in gm/dl)
33	PMS	Partial mayo score 0-PMS 0, 1-PMS 1
34	MES	Mayo endoscopic score 0-MES 0; 1-MES 1; 2-MES 2; 3-MES-3
35	UCEIS	Ulcerative colitis endoscopic index of severity 0-UCEIS 0; 1-UCEIS 1; 2-UCEIS 2; 3-UCEIS 3, 4-UCEIS-4; 5-UCEIS 5
36	LCI	Linked color imaging 1-LCI A; 2-LCI B; 3-LCI C
37	NHI	Nancy histological index 0-NHI 0; 1-NHI 1; 2-NHI 2; 3-NHI 3; 4-NHI 4
38	5 ASA (Oral)	History of 5-Aminosalicylic acid(oral) received in past 0-Not received; 1-Received

39	Azathioprine	History of azathioprine received in past 0-Not received; 1-Received
40	6-MP	History of 6-Mercaptopurine received in past 0-Not received; 1-Received
41	Tofacitinib	History of Tofacitinib received in past 0-Not received; 1-Received
42	Biological	History of biologics received in past 0-Not received; 1-Received
43	Steroid	History of steroid (oral) received in past 0-Not received; 1-Received
44	FMT	History of fecal microbiota transplant received in past 0-Not received; 1-Received
45	Steroid (Rectal)	History of steroid (rectal) received in past 0-Not received; 1-Received
46	5-ASA(Rectal)	History of 5-Aminosalicylic acid(rectal) received in past 0-Not received; 1-Received
47	Current treatment	Current treatment history 1- Oral 5-Aminosalicylic acid 2- Oral 5-Aminosalicylic acid + Rectal 5-Aminosalicylic acid 3- Oral 5-Aminosalicylic acid + Immunomodulators (Azathioprine and 6-MP) 4 - Oral 5-Aminosalicylic acid + Tofacitinib 5- Oral 5-Aminosalicylic acid + Tofacitinib + Rectal 5-Aminosalicylic acid 6- Oral 5-Aminosalicylic acid + Immunomodulator (Azathioprine and 6-MP) + Rectal 5-Aminosalicylic acid

48	L	Lab value in Adobe Photoshop color space “L” represent lightness, ranges from 0 to 100 0-Black ; 100-White
49	a	Lab value in Adobe Photoshop color space “a” represent red-green axis, ranges from -128 to +127 Negative value indicates green; positive value indicates red
50	b	Lab value in Adobe Photoshop color space “b” represent blue yellow axis, ranges from -128 to +127 Negative value indicates blue; positive value indicates yellow
51	LCI index	Represent CIELAB “a” value, derived from formula [Photoshop a -value/128) × 120] Ranges from -120 to + 120 Negative value indicates green; positive value indicates red
52	R	Lab value in Adobe Photoshop color space “R” represent amount of red, ranges from 0 to 255
53	G	Lab value in Adobe Photoshop color space “G” represent amount of green, ranges from 0 to 255
54	B	Lab value in Adobe Photoshop color space “B” represent amount of blue, ranges from 0 to 255

S no.	MRD	Initials	Age	Sex	Hypertension	Diabetes	Coronary artery disease	Hypothyroid	Cerebrovascular disease	Alcohol use	Smoking	Age at onset of symptoms	Age at diagnosis	Year of diagnosis
1	1512403	SS	24	M	0	0	0	0	0	0	0	23	23	2023
2	901533	SK	24	F	0	0	0	0	0	0	0	14	14	2014
3	459437	RD	59	F	0	0	0	0	0	0	0	53	53	2016
4	1138957	JS	25	M	0	0	0	0	0	0	0	24	24	2020
5	720747	GS	35	M	0	0	0	0	0	0	0	22	22	2010
6	1282610	RK	38	M	0	0	0	0	0	0	0	35	35	2023
7	90050	BR	46	F	0	0	0	0	0	0	0	32	32	2009
8	212286	AK	55	M	1	1	0	0	0	0	0	34	34	2003
9	1187263	AS	23	M	0	0	0	0	0	0	0	21	21	2021
10	734676	JS	39	M	0	0	0	0	0	0	0	35	35	2019
11	1228713	RK	32	F	0	0	0	0	0	0	0	26	27	2017
12	554664	KG	42	F	0	0	0	0	0	0	0	40	41	2022
13	960943	SS	34	M	0	0	0	0	0	0	0	30	32	2020
14	1343210	KS	52	M	0	0	0	0	0	1	0	45	51	2022
15	181979	S	45	F	0	0	0	0	0	0	0	35	35	2014
16	1173421	GK	40	M	0	0	0	0	0	0	0	37	37	2020
17	959816	HS	22	M	0	0	0	0	0	0	0	18	18	2019
18	421990	RG	17	M	0	0	0	0	0	0	0	11	11	2017
19	1060435	SK	42	F	0	0	0	0	0	0	0	40	40	2021
20	325682	SK	43	F	0	0	0	0	0	0	0	18	18	1998
21	1466136	BM	62	M	1	1	1	0	0	0	0	60	62	2023
22	478111	HS	40	M	0	0	0	0	0	0	0	35	35	2018
23	1357950	DK	51	M	0	0	1	0	0	0	0	48	51	2020
24	25442	JK	37	F	0	0	0	0	0	0	0	29	29	2014
25	234804	NG	25	F	1	0	0	0	0	0	0	50	55	2015
26	809449	RS	31	M	0	0	0	0	0	0	0	19	19	2011
27	683680	JK	69	M	0	0	0	1	1	1	1	59	59	2014
28	1021077	KK	36	F	0	0	0	0	0	0	0	33	34	2021
29	105475	RKG	28	M	0	0	0	0	0	0	0	17	17	2012
30	1329009	HS	35	M	0	0	0	0	0	0	0	34	34	2022
31	1204825	JK	43	F	0	0	0	0	0	0	0	38	38	2018
32	356499	MB	42	M	0	0	0	0	0	0	0	25	25	2006
33	552361	PS	33	M	0	0	0	0	0	0	0	23	24	2014
34	1201561	SC	47	M	0	0	0	0	0	0	0	42	42	2016
35	1141123	CK	38	F	0	0	0	0	0	0	0	37	37	2021
36	1485263	R	27	M	0	0	0	0	0	0	0	26	26	2022
37	773605	SK	32	F	0	0	0	0	0	0	0	26	27	2019
38	1343657	LK	20	M	0	0	0	0	0	0	0	18	18	2021
39	1551382	MK	36	F	0	0	0	0	0	0	0	32	32	2019
40	870561	MK	30	F	0	0	0	0	0	0	0	26	26	2019
41	200254	GS	51	M	0	0	0	0	0	0	0	41	41	2013
42	431334	GS	27	M	0	0	0	0	0	0	0	18	18	2014
43	1357950	DK	51	M	0	0	1	0	0	0	0	48	48	2020
44	1174670	AG	41	M	1	0	0	0	0	0	0	37	37	2019
45	31810	BR	47	M	0	0	0	0	0	0	0	37	37	2013
46	105975	NK	52	F	0	0	0	0	0	0	0	42	42	2014
47	1378913	BM	27	M	0	0	0	0	0	0	0	25	25	2021
48	1169193	AS	24	F	0	0	0	0	0	0	0	22	22	2019
49	1242107	BK	58	F	0	0	0	0	0	0	0	53	53	2019
50	1364434	RKB	34	M	0	0	0	0	0	0	0	30	30	2019
51	1367713	RR	47	F	0	0	0	0	0	0	0	46	46	2022
52	944308	VS	44	M	0	0	0	0	0	0	0	31	31	2009

S no.	MRD	Initials	Disease duration	Disease Extent	Family History of IBD	Height	Weight	BMI	MUAC	Hand grip strength	Hemoglobin	PCV	MCV	TLC	Platelets	ESR	CRP	FC	Albumin	PMS	MES	UCEIS	LCI	NHI
1	1512403	SS	1	2	0	180	58.4	17.9	20	12	11.5	34.8	83.8	10	190	12	1.1	25	3.82	0	0	0	2	4
2	901533	SK	10	2	1	154	56	24	27	20	10.2	32.1	78.9	7.2	382	6	0.5	43	3.36	0	2	3	3	1
3	459437	RD	7	1	0	155	76	32	31	24	9.9	32	87	7.9	150	26	2.1	25	4.12	1	0	0	1	0
4	1138957	JS	3	2	0	182	68	20	26	39	13.1	42.6	84	5.4	187	6	5.1	25	3.4	0	0	0	1	0
5	720747	GS	13	2	0	176	75	24	28	31	15.8	48.9	86	10.8	304	2	0.5	100	4.7	0	1	1	2	0
6	1282610	RK	1	2	0	170	62	22	28	26	14.7	40.6	88.2	5.6	206	4	0.6	25	3.9	0	1	2	3	1
7	90050	BR	14	2	0	155	45	21	25.9	13	10.1	34.5	78.2	4.4	302	10	5.8	33	3.2	0	1	2	3	2
8	212286	AK	21	2	0	170	67	23	25	32	10.8	34.9	73.2	5.6	108	12	10.1	25	3.64	0	2	3	3	3
9	1187263	AS	3	2	0	178	76	23	29.8	42	14.9	46.3	88.1	7.6	224	8	2.1	134	4.1	0	0	0	1	0
10	734676	JS	4	2	0	167	71	25	30	46	10.9	35	69.5	5.5	172	10	1	157	4.6	1	1	1	2	0
11	1228713	RK	6	2	0	173	76	25	29.4	26	12	39.4	76.1	4.9	245	9	1.8	25	3.9	0	0	0	1	0
12	554664	KG	1	2	0	168	58	20.7	24	26	10.8	28.6	87.4	8.4	208	12	1.6	25	3.4	0	1	1	3	3
13	960943	SS	3	2	0	168	52	18	24	40	10.5	31.8	79.4	6.9	324	4	3.1	175	3.12	0	0	0	2	3
14	1343210	KS	7	2	0	173	74	25	29	32	11.2	36.1	81.4	6.4	228	6	4.1	56	3.86	0	1	1	3	1
15	181979	S	9	1	1	152	54	24	25	24	13.4	40.8	86	8	171	12	10.1	25	3.74	0	1	1	2	1
16	1173421	GK	3	3	0	166	49	18	22	40	12.3	35.6	68.6	7.4	167	10	8.1	61	2.96	0	0	0	1	1
17	959816	HS	4	2	0	170	53	18	26	48	14	42.3	98.9	5.8	132	5	0.4	25	3.24	0	0	0	1	1
18	421990	RG	6	2	0	178	79	25	30	40	16.4	40.2	88.4	7.6	338	6	2	25	4.6	1	2	3	3	3
19	1060435	SK	2	1	0	160	61	24	26.8	11	8.9	28.1	68.9	4.1	285	18	2.1	135	3.84	1	0	0	2	3
20	325682	SK	25	3	0	159	52	20	25	23	9.8	32.1	82.5	6.7	233	21	1.4	156	3.24	1	1	1	2	3
21	1466136	BM	2	2	0	162	62	26	24	29	12.1	38.9	85.1	7.6	204	10	3.2	113	3.68	1	3	5	3	3
22	478111	HS	5	1	0	168	74	26	29.5	41	13.9	41.9	78.9	7.8	179	8	2.3	25	4.26	0	0	0	1	0
23	1357950	DK	3	2	0	174	108	34	34	27	10.8	38	97	5.8	202	14	1.6	25	3.98	0	1	1	2	0
24	25442	JK	9	2	0	168	66	23.5	24	28	12.4	32.1	86.4	4.7	276	9	1.1	25	4.1	0	0	0	1	1
25	234804	NG	8	2	0	157	65	26	28.5	12	14.1	44.2	82.1	5.4	178	4	7.2	25	4.25	0	0	0	1	0
26	809449	RS	12	2	0	169	58	20	26	50	10.9	32.9	81.2	6.7	298	12	0.9	136	3.84	1	2	4	3	3
27	683680	JK	9	2	0	174	63	20.8	24	20	12.9	29.3	87.5	9.1	49	25	3.4	25	3.6	0	0	0	1	1
28	1021077	KK	3	1	0	170	75	26	27	31	13.4	32	109	6.9	217	10	0.7	25	4.38	0	0	0	1	0
29	105475	RKG	11	3	0	178	54	17	21.6	43	15.9	46	84	5.1	253	6	0.67	25	3.14	0	0	0	1	0
30	1329009	HS	1	2	1	172	76	26	28	45	15.5	47.5	93.5	7	172	3	1.2	43	4.8	0	0	0	1	0
31	1204825	JK	5	2	0	153	62	27	30	28	10.7	28.4	90.5	6	256	16	2.8	51	4.05	0	0	0	1	0
32	356499	MB	17	1	0	175	51	17	24	42	12.9	35.5	97	4.9	205	8	1	373	3.02	0	0	0	2	0
33	552361	PS	9	2	0	180	56	17.3	25.2	22	14.7	43.6	88.9	9.4	400	5	0.8	25	2.94	1	1	2	3	3
34	1201561	SC	7	1	0	167	84	30	31.2	44	12.8	40.2	82.6	4.6	192	8	1.4	25	4.42	0	0	0	1	0
35	1141123	CK	2	2	0	151	64	28	29.2	22	10.9	36.1	80.4	5.4	328	19	6.1	221	4.16	0	2	5	3	4
36	1485263	R	1	2	0	182	87	26	31	22	9.8	30.2	78.1	4.4	222	24	3.1	319	4.5	1	0	0	1	0
37	773605	SK	5	3	0	164	65	24	27	27	12.7	38.1	82.4	9.1	176	18	1.2	26	3.46	0	0	0	1	0
38	1343657	LK	2	1	0	183	62	18.6	25	33	14.7	46	88	5.2	150	4	0.2	25	3.21	0	0	0	2	0
39	1551382	MK	4	1	0	165	48	18	24	29	11.6	36	87	8.1	439	5	1.1	84	3.06	0	0	0	1	0
40	870561	MK	4	2	0	152	40	17	18	26	10.8	32.1	72.4	5.8	204	18	0.9	25	3.84	0	0	0	1	0
41	200254	GS	10	3	0	165	73	26	27.8	42	14.1	44.3	86.4	7.6	156	9	1.5	25	4.62	0	0	0	1	0
42	431334	GS	9	2	0	180	75	23	31	41	12.9	40.1	82.9	5.6	178	7	6.5	56	3.98	0	0	0	1	0
43	1357950	DK	3	2	0	174	104	34	34	27	14.2	46.5	84.6	9.1	202	5	3.2	25	4.14	0	0	1	2	0
44	1174670	AG	5	2	0	167	74	27	268	32	15.2	44.2	88.1	7.2	297	4	0.56	25	3.86	1	0	1	2	2
45	31810	BR	10	2	0	178	70	22	26.5	30	11.7	37.1	79.8	5.1	206	10	5.7	25	3.92	0	1	1	1	0
46	105975	NK	10	1	0	155	60	26	26.8	14	12.7	40.7	93	5.5	160	26	4.4	54	4.18	0	0	0	1	0
47	1378913	BM	2	2	0	168	63	22	26	40	15.2	45.4	82	7.6	168	14	1.4	25	3.54	0	1	1	2	3
48	1169193	AS	5	1	0	158	53	21	24.6	12	12.2	36.4	79.1	8.2	208	12	1.2	25	3.22	0	0	0	1	0
49	1242107	BK	5	2	0	147	51	23	28	20	11.4	36.9	94.4	5.7	265	21	0.7	25	3.96	0	0	0	1	1
50	1364434	RKB	4	2	0	172	62	22.6	32	35	11.6	39.8	79.4	8.1	248	24	10.1	25	4.19	0	0	0	1	0
51	1367713	RR	1	2	0	159	56	22	25	16	11.5	35.4	82.4	4.6	209	17	2.1	35	3.48	0	0	0	1	0
52	944308	VS	14	2	0	165	82	30.2	28	32	14.2	41.8	90.5	6.4	198	8	0.68	161	4.26	1	1	1	1	0

S no.	MRD	Initials	5 ASA (Oral)	Azathioprine	6-MP	Tofacitinib	Biological	Steroid	FMT	Steroid(Rectal)	5-ASA(Rectal)	Current treatment	L	a	b	LCI index	R	G	B
1	1512403	SS	1	0	0	0	0	1	0	0	1	2	47	33	16	31.5	166	88	86
2	901533	SK	1	1	0	0	0	1	0	0	0	3	48	48	27	45	191	73	71
3	459437	RD	1	0	0	0	0	0	0	0	0	1	53	12	22	11.25	156	119	89
4	1138957	JS	1	0	0	1	0	1	0	0	0	4	41	24	11	22.5	137	80	79
5	720747	GS	1	1	0	0	0	1	0	0	0	4	46	32	2	30	158	86	106
6	1282610	RK	1	0	0	0	0	0	0	0	1	2	28	31	10	29.06	111	44	53
7	90050	BR	1	1	0	0	0	1	0	1	1	3	48	44	33	41.25	186	77	61
8	212286	AK	1	0	0	0	0	0	1	0	1	1	40	52	19	48.75	172	46	67
9	1187263	AS	1	0	0	0	0	0	0	0	1	2	41	10	6	9.38	116	91	88
10	734676	JS	1	0	0	0	0	1	0	0	1	2	38	38	16	35.63	147	60	65
11	1228713	RK	1	0	0	0	0	0	0	0	0	1	54	12	22	11.25	157	120	91
12	554664	KG	1	0	0	0	0	0	0	0	1	2	49	32	23	30	171	92	79
13	960943	SS	1	0	0	1	0	1	0	0	1	5	51	41	12	38.44	189	91	105
14	1343210	KS	1	1	0	0	0	0	0	0	1	3	47	46	27	43.13	185	73	69
15	181979	S	1	0	0	0	0	1	1	0	0	1	47	35	21	32.81	170	85	78
16	1173421	GK	1	0	1	0	0	0	0	0	1	3	48	19	8	17.81	147	101	100
17	959816	HS	1	0	0	0	0	1	0	0	0	3	48	14	13	13.13	141	105	93
18	421990	RG	1	1	0	0	0	0	0	0	1	3	43	49	28	46.04	176	57	58
19	1060435	SK	1	0	0	0	0	0	0	0	0	1	27	36	33	33.75	118	35	15
20	325682	SK	1	0	0	1	0	0	0	0	1	5	40	31	16	29.06	143	71	69
21	1466136	BM	1	0	0	1	0	0	0	0	1	5	44	50	42	46.88	182	59	37
22	478111	HS	1	0	0	0	0	0	0	0	1	2	51	6	17	5.63	140	118	94
23	1357950	DK	1	1	0	1	0	1	0	0	1	4	49	45	31	42.19	192	80	67
24	25442	JK	1	0	0	0	0	0	0	0	0	1	48	19	8	17.81	147	101	100
25	234804	NG	1	0	0	0	0	0	0	0	1	1	45	4	20	3.75	122	105	75
26	809449	RS	1	1	0	1	0	1	0	0	1	5	44	50	38	46.88	183	60	45
27	683680	JK	1	1	0	0	0	0	0	0	0	1	48	17	31	15.94	151	103	62
28	1021077	KK	1	0	0	0	0	0	0	0	0	1	55	21	19	19.69	174	118	100
29	105475	RKG	1	1	0	1	0	1	0	0	1	5	37	24	13	22.5	126	71	68
30	1329009	HS	1	0	0	0	0	0	0	1	1	1	51	23	29	21.56	166	105	73
31	1204825	JK	1	0	0	1	0	0	0	0	0	4	47	24	14	22.5	155	96	91
32	356499	MB	1	1	0	0	0	1	1	0	0	3	31	42	30	39.38	133	35	28
33	552361	PS	1	0	0	1	0	1	0	0	0	4	30	47	33	44.07	138	25	24
34	1201561	SC	1	0	0	1	0	1	0	0	0	4	50	20	29	18.75	160	104	69
35	1141123	CK	1	0	0	1	0	0	0	0	1	4	42	59	53	55.31	189	36	10
36	1485263	R	1	0	0	1	0	1	0	0	0	4	41	15	11	14.07	124	86	78
37	773605	SK	1	0	0	0	0	0	0	0	0	1	51	20	23	18.75	163	109	84
38	1343657	LK	1	1	0	0	0	0	0	0	1	3	38	48	29	45	162	45	46
39	1551382	MK	1	0	0	0	0	0	0	0	1	2	49	25	29	23.44	164	98	68
40	870561	MK	1	0	0	0	0	0	0	0	0	1	43	8	15	7.5	120	96	76
41	200254	GS	1	0	0	1	0	0	0	0	0	4	57	20	21	18.75	179	124	102
42	431334	GS	1	1	0	0	0	0	0	0	0	1	47	26	13	24.38	157	94	91
43	1357950	DK	1	0	0	0	0	0	0	0	1	1	48	43	30	40.31	185	80	67
44	1174670	AG	1	1	0	1	1	1	0	1	1	4	51	39	19	36.56	186	92	92
45	31810	BR	1	0	0	0	0	0	0	0	0	1	53	7	21	6.56	147	122	91
46	105975	NK	1	0	0	0	0	0	0	0	0	1	59	2	21	1.88	155	139	105
47	1378913	BM	1	1	0	1	0	0	0	0	0	4	36	49	21	46.24	154	38	54
48	1169193	AS	1	0	0	1	0	1	0	0	0	4	53	11	16	10.31	152	119	100
49	1242107	BK	1	0	0	1	0	1	0	0	0	4	50	21	13	19.69	158	105	99
50	1364434	RKB	1	0	0	1	0	0	0	0	0	4	44	11	17	10.31	129	97	76
51	1367713	RR	1	1	0	0	0	1	0	0	0	2	35	14	10	13.13	107	73	67
52	944308	VS	1	0	0	1	0	0	0	0	1	5	46	23	22	21.56	151	93	73

S no.	MRD	Initials	Age	Sex	Hypertension	Diabetes	Coronary artery disease	Hypothyroid	Cerebrovascular disease	Alcohol use	Smoking	Age at onset of symptoms	Age at diagnosis	Year of diagnosis
53	1598856	MS	26	M	0	0	0	0	0	0	0	25	25	2022
54	1337808	SK	35	M	0	0	0	0	0	0	0	34	34	2022
55	51414	GS	33	M	0	0	0	0	0	0	0	20	21	2011
56	1113989	RK	37	F	0	0	0	0	0	0	0	33	33	2019
57	1389274	JS	46	M	0	0	0	0	0	0	0	45	45	2022
58	160216	A	56	F	0	0	0	0	0	0	0	37	38	2002
59	1223222	RK	50	F	0	0	0	0	0	0	0	48	48	2021
60	1338938	SK	25	M	0	0	0	0	0	0	0	22	22	2020
61	661408	SB	52	M	0	0	0	0	0	0	0	45	45	2018
62	1525276	NS	44	M	0	0	0	0	0	0	0	36	37	2017
63	699032	SJ	50	M	0	0	0	0	0	0	0	26	27	1998
64	642786	SS	46	M	0	0	0	0	0	0	0	38	40	2018
65	1283545	JK	33	F	0	0	0	0	0	0	0	23	24	2013
66	1301758	GB	31	M	0	0	0	0	0	0	0	29	29	2022
67	1428588	HS	29	M	0	0	0	1	0	0	0	27	27	2022
68	505801	BS	46	M	0	0	0	0	0	0	0	10	36	2013
69	80817	AK	25	F	0	0	0	0	0	0	0	14	14	2013
70	1433285	NS	34	F	0	0	0	0	0	0	0	30	31	2021
71	1261394	KK	34	F	0	0	0	0	0	0	0	31	31	2021
72	85897	BK	57	F	0	0	0	0	0	0	0	37	37	2004
73	505803	TS	36	M	0	0	0	0	0	0	0	31	31	2018
74	51513	MS	29	M	0	0	0	0	0	0	0	16	16	2010
75	154608	MR	45	M	0	0	0	0	0	0	0	22	22	2001
76	1298905	HK	30	F	0	0	0	0	0	0	0	22	22	2015
77	1141268	NK	29	M	0	0	0	0	0	0	0	26	26	2021
78	890074	JK	56	M	0	0	0	0	0	0	0	52	52	2020
79	1148303	MA	29	M	0	0	0	0	0	0	0	24	24	2018
80	1470356	SS	32	M	0	0	0	0	0	0	0	30	30	2022
81	675741	DS	27	M	0	0	0	0	0	0	0	22	22	2019
82	1574791	MS	18	M	0	0	0	0	0	0	0	18	18	2023
83	1679899	A	23	M	0	0	0	0	0	0	0	19	19	2019
84	983460	PG	27	F	0	0	0	1	0	0	0	20	26	2022
85	983460	D	36	M	0	0	0	0	0	0	0	34	34	2022
86	151076	SN	60	M	0	0	0	0	0	0	0	50	50	2014
87	97833	BS	55	M	0	0	0	0	0	0	0	22	23	1992
88	1026008	SS	44	M	0	0	0	0	0	0	0	41	41	2021
89	1129496	SK	52	F	0	0	0	0	0	0	0	42	42	2010
90	752767	RK	20	F	0	0	0	0	0	0	0	14	14	2018
91	572226	GS	55	M	0	0	0	0	0	0	0	41	42	2010
92	733160	HK	64	F	0	0	0	0	0	0	0	57	57	2019
93	1726097	E	30	F	0	0	0	0	0	0	0	18	18	2012
94	1030924	AS	58	M	0	0	0	0	0	0	0	50	52	2018
95	1282818	MP	31	F	0	0	0	0	0	0	0	29	29	2022
96	1513423	RV	48	M	0	0	0	0	0	0	0	32	33	2023
97	1569997	AK	60	M	0	0	0	0	0	0	0	56	56	2020
98	1721304	P	20	M	0	0	0	0	0	0	0	15	15	2019
99	208593	HK	46	F	0	0	0	0	0	0	0	24	26	2004
100	764251	MB	35	F	0	0	0	0	0	0	0	27	28	2018
101	1649897	SK	55	F	0	0	0	0	0	0	0	48	48	2016
102	1727741	PK	35	F	0	0	0	0	0	0	0	34	35	2024
103	1716907	KS	41	M	0	0	0	0	0	0	0	27	27	2010

S no.	MRD	Initials	Disease duration	Disease Extent	Family History of IBD	Height	Weight	BMI	MUAC	Hand grip strength	Hemoglobin	PCV	MCV	TLC	Platelets	ESR	CRP	FC	Albumin	PMS	MES	UCEIS	LCI	NHI
53	1598856	MS	1	2	0	167	58	20.9	24	26	12.9	38.3	87.4	4.4	150	19	0.3	39	4.15	0	0	0	1	0
54	1337808	SK	1	2	0	172	78.3	26.5	32	43	14.1	44.2	83.8	7.3	287	24	0.6	25	4.68	0	0	0	1	0
55	51414	GS	12	2	0	175	81	26.4	29	56	14.4	46.3	92.1	6.3	239	8	1.7	33	3.58	0	0	0	1	0
56	1113989	RK	4	2	0	151	49	21.6	24	18	12.2	39.1	89.4	4.1	186	6	4.7	184	4.18	0	0	0	1	0
57	1389274	JS	1	2	0	180	69.7	21.4	26	40	14.6	42.7	79.8	7.4	176	7	0.8	25	3.48	0	0	0	1	1
58	160216	A	22	2	0	154	57	24	26	20	10.9	38.1	80.2	6.3	204	18	1.3	88	3.98	0	0	0	2	2
59	1223222	RK	2	1	0	177	60	19.3	28	33	14.9	45.4	84.2	4.7	152	4	2.5	38	4.5	0	0	0	1	0
60	1338938	SK	3	3	0	182	66	20.1	26	40	9.2	32.1	78.3	8.4	298	26	6.4	74	3.26	0	0	0	2	3
61	661408	SB	6	3	0	168	85	30.1	30	36	15	45	92.2	7.2	213	12	1.2	25	4.1	0	0	0	1	1
62	1525276	NS	7	2	0	170	83	28	31	38	11.3	35.8	76.1	6.8	172	16	0.8	25	3.25	0	0	0	1	0
63	699032	SJ	27	2	0	170	69	24	28	29	11.9	36.6	97	5.9	215	19	7.1	25	4.87	0	0	0	1	0
64	642786	SS	6	2	0	172	78	26	32	44	12.1	40.1	86.8	7.1	192	4	1.5	25	3.94	0	0	0	1	0
65	1283545	JK	10	2	0	166	63	23.1	28	33	13.6	41.5	85.9	7.2	309	10	2	25	3.48	0	0	0	1	1
66	1301758	GB	1	3	0	163	79	29.7	32	34	12	38	89.8	5.2	256	14	4	25	3.6	0	1	1	2	3
67	1428588	HS	2	2	0	173	57.7	19.4	24	20	13.7	41.2	90.9	4.2	160	2	0.88	25	3.5	0	0	0	1	1
68	505801	BS	10	2	0	165	66.3	24.3	26	39	14.4	45.5	88.8	10.3	128	12	0.32	38	4.1	0	0	0	2	3
69	80817	AK	10	1	0	168	71.6	23.4	28	26	12.2	39.9	92.1	7.4	182	21	1.2	25	3.48	0	0	0	1	1
70	1433285	NS	3	1	0	166	54.6	20.2	23	24	9.2	28.1	78.2	7	166	18	0.7	25	4.1	0	2	3	3	0
71	1261394	KK	3	2	0	150	36.7	16	22	30	10.9	32.1	96.3	4.9	272	9	5.7	25	3.01	0	3	5	3	3
72	85897	BK	20	2	0	154	78	33	28	22	11.4	36.6	71.3	9.9	329	4	2.6	25	3.94	0	0	0	1	1
73	505803	TS	5	1	0	174	60	19.8	24	32	12	34.1	88.2	7.4	201	12	3.7	59	3.15	0	0	0	2	2
74	51513	MS	13	1	0	174	78	25.8	32	50	11.1	37.2	78.1	4.1	209	21	8.4	25	4.1	0	0	0	2	2
75	154608	MR	23	1	0	174	50	16.5	21	30	9.4	32.1	76.4	8.4	294	19	2	31	3.28	1	0	0	1	1
76	1298905	HK	8	2	0	175	62.8	20.5	21	25	10.6	32.5	78	10.4	456	24	0.7	252	3.16	1	0	0	2	3
77	1141268	NK	3	2	0	180	77.8	24	28	30	12.9	39.1	92.4	4.7	210	8	9	25	3.48	0	1	1	1	1
78	890074	JK	4	3	0	154	50	21.5	26	30	12.8	40	92.1	7.2	347	14	1.8	36	4.2	1	0	0	2	3
79	1148303	MA	5	2	0	157	64	26	30	28	13.2	41.3	79	5.4	109	15	2.1	25	4.25	0	0	0	1	0
80	1470356	SS	2	2	0	172	72	22	24	30	10.1	32.1	80.1	9.4	332	26	6.2	112	3.65	0	1	2	3	3
81	675741	DS	5	2	0	178	81	25.6	26	40	12.7	40.2	92.1	4.8	248	4	1.4	39	4.42	0	0	0	1	0
82	1574791	MS	1	2	0	168	42	14.9	24	20	13.5	39.2	85.2	7.2	297	2	0.2	25	2.98	0	1	1	1	1
83	1679899	A	4	3	0	181	62	19	26	30	13.7	42.7	82.9	7.5	303	16	1.2	65	3.09	0	1	2	3	3
84	983460	PG	2	3	0	157	54.2	22.2	26	16	12.2	32.6	84.2	6.2	234	9	1.4	36	4.2	0	1	2	3	3
85	983460	D	20	2	0	170	80	27.1	30	40	10.5	34.1	88.6	6.4	184	17	0.5	42	3.58	0	0	0	1	0
86	151076	SN	10	2	0	172	72	22	28	22	10.9	37.4	71	4.8	341	15	2	88	4.1	0	1	1	1	0
87	97833	BS	32	2	0	179	84	27.3	30	24	12.1	40.2	82.1	8.4	242	2	8	36	4.08	0	0	0	1	0
88	1026008	SS	3	2	0	168	72	25.5	32	48	10.2	36.1	79.2	9.1	396	8	12	2000	3.24	0	2	4	3	4
89	1129496	SK	14	2	0	154	52	22	21	24	9.4	32.1	80.2	5.8	348	14	1.2	258	3.8	0	3	5	3	4
90	752767	RK	6	2	0	162	48	18.4	19	20	11.7	38.5	75.9	7.32	285	12	2	52	3.4	0	0	0	1	0
91	572226	GS	14	2	0	178	92	29	32	35	14.9	43.1	83.8	6.62	262	5	5.1	203	4.52	0	0	0	1	0
92	733160	HK	5	2	0	159	57	22	28	17	13.5	42.9	77.1	7.5	184	3	6.4	25	4.12	0	1	1	1	0
93	1726097	E	12	2	0	160	39	15	22	19	9.4	29.5	79.1	8.7	346	11	0.11	314	2.86	1	3	5	3	4
94	1030924	AS	6	2	0	156	60	24	28	25	11.5	35.9	92.9	4.31	150	8	0.6	25	3.49	0	0	0	1	0
95	1282818	MP	2	2	0	158	65	26	23	20	12.9	39.5	82.4	5.8	348	6	1.8	496	4.27	0	0	0	2	3
96	1513423	RV	1	1	0	169	59	22	24	34	10.1	34.5	78.9	7.4	196	14	2.1	109	4.19	0	0	1	1	0
97	1569997	AK	4	2	0	168	71	25	30	23	11.2	34.5	81.9	4.7	172	12	6.1	28	3.95	0	1	1	2	3
98	1721304	P	5	3	0	182	76	23	30	30	15.4	48	84.6	6.79	188	4	0.6	107	3.98	0	1	2	1	0
99	208593	HK	20	2	0	160	64	25	22	15	9.9	31.4	81.9	8.19	230	10	1.1	56	4.24	0	0	0	2	4
100	764251	MB	6	2	0	157	48	17.4	21	14	9.4	30.2	78.4	9.1	352	21	5.8	155	2.98	0	2	3	3	3
101	1649897	SK	8	2	0	162	62	23.9	28	30	12.1	39.2	82.4	4.7	164	4	4.7	25	3.15	0	1	1	1	0
102	1727741	PK	0.6	1	0	166	58	21	26	24	11.9	36.4	84.1	5.9	302	5	1.1	105	3.48	0	1	1	2	3
103	1716907	KS	14	1	0	168	55	19.5	28	30	12.4	43.2	100.2	7.9	144	12	0.9	25	3.96	0	0	0	1	0

S no.	MRD	Initials	5 ASA (Oral)	Azathioprine	6-MP	Tofacitinib	Biological	Steroid	FMT	Steroid(Rectal)	5-ASA(Rectal)	Current treatment	L	a	b	LCI index	R	G	B
53	1598856	MS	1	0	0	0	0	0	0	0	0	1	57	21	24	19.69	180	123	96
54	1337808	SK	1	0	0	1	0	1	0	0	1	5	61	21	24	19.69	193	133	107
55	51414	GS	1	1	0	0	0	1	0	0	1	6	50	25	21	23.44	165	102	85
56	1113989	RK	1	0	0	1	0	0	0	0	0	4	67	15	15	14.07	195	152	135
57	1389274	JS	1	0	0	0	0	0	0	0	1	2	55	21	26	19.69	174	117	88
58	160216	A	1	1	0	0	0	1	0	0	1	6	51	48	42	45	202	81	52
59	1223222	RK	1	0	0	0	0	0	0	0	1	2	76	13	24	12.19	220	177	142
60	1338938	SK	1	0	0	1	0	1	0	0	0	4	55	63	46	59.06	235	72	57
61	661408	SB	1	0	0	1	0	1	0	0	0	3	73	20	30	18.75	226	164	125
62	1525276	NS	1	0	0	0	0	0	0	0	0	1	51	11	23	10.31	148	113	81
63	699032	SJ	1	0	0	1	0	0	0	0	0	1	62	18	21	16.88	188	136	113
64	642786	SS	1	0	0	0	0	0	0	0	0	1	48	18	11	16.88	147	102	96
65	1283545	JK	1	0	0	0	0	0	0	0	1	2	60	9	26	8.44	170	138	99
66	1301758	GB	1	0	0	1	0	1	0	0	1	5	52	47	48	44.07	204	85	42
67	1428588	HS	1	0	0	1	0	1	0	0	1	5	65	19	29	17.81	203	145	108
68	505801	BS	1	0	0	1	0	0	0	1	1	5	50	55	30	51.56	207	71	73
69	80817	AK	1	0	0	0	0	0	1	0	0	1	54	3	20	2.81	142	126	93
70	1433285	NS	1	1	0	0	0	0	0	0	1	3	54	55	47	51.56	220	79	51
71	1261394	KK	1	0	1	0	0	1	0	0	1	3	46	55	44	51.56	197	57	40
72	85897	BK	1	0	0	0	0	0	0	0	0	1	87	10	42	9.38	255	209	137
73	505803	TS	1	1	0	0	0	1	0	0	1	6	54	39	25	36.56	197	99	88
74	51513	MS	1	1	0	0	0	1	0	0	0	3	35	39	31	36.56	143	50	35
75	154608	MR	1	0	0	0	0	0	0	0	0	1	53	22	35	20.63	172	111	67
76	1298905	HK	1	1	0	0	0	1	0	0	9	5	54	48	37	45	210	88	67
77	1141268	NK	1	0	0	1	0	0	0	0	0	4	60	15	33	14.07	183	135	87
78	890074	JK	1	0	0	0	0	1	0	0	1	1	43	19	12	17.81	137	90	84
79	1148303	MA	1	0	0	1	0	0	0	0	0	4	62	16	28	15	188	138	101
80	1470356	SS	1	0	0	1	0	0	0	0	0	4	51	60	36	56.25	217	64	66
81	675741	DS	1	0	0	0	0	0	0	0	0	1	51	11	21	10.31	149	115	87
82	1574791	MS	1	0	0	0	0	0	0	0	0	1	59	23	20	21.56	188	127	109
83	1679899	A	1	0	0	0	0	0	0	0	0	2	51	60	36	56.25	217	64	66
84	983460	PG	1	0	0	0	0	0	0	0	1	2	47	55	39	51.56	198	60	50
85	983460	D	1	0	0	0	0	0	0	0	0	1	61	23	39	21.6	199	132	79
86	151076	SN	1	1	0	0	0	1	0	0	1	3	63	10	31	9.38	183	145	98
87	97833	BS	1	0	0	1	0	0	0	0	1	4	39	24	34	22.5	137	75	36
88	1026008	SS	1	0	0	0	0	1	0	0	1	2	57	56	44	52.5	230	86	62
89	1129496	SK	1	0	0	0	0	1	0	0	1	1	37	49	43	46.01	160	39	18
90	752767	RK	1	0	0	1	0	0	0	0	0	4	64	23	26	21.56	205	140	112
91	572226	GS	1	0	0	1	0	0	0	0	0	4	62	17	31	15.94	191	138	96
92	733160	HK	1	0	0	0	0	0	0	0	0	1	25	18	22	16.88	88	47	25
93	1726097	E	1	0	0	0	0	1	0	0	1	1	36	53	49	49.69	162	28	3
94	1030924	AS	1	0	0	1	0	0	0	0	0	4	50	9	25	8.44	142	112	76
95	1282818	MP	1	0	0	0	0	0	0	0	1	1	43	46	35	43.13	175	62	46
96	1513423	RV	1	0	0	0	0	0	0	0	0	1	70	19	28	17.81	215	157	120
97	1569997	AK	1	0	0	1	0	1	0	0	1	4	56	60	54	56.25	235	78	43
98	1721304	P	1	1	0	0	0	1	0	0	1	3	73	18	28	16.88	223	167	130
99	208593	HK	1	1	0	0	0	1	0	0	1	3	55	52	8	48.75	214	89	121
100	764251	MB	1	0	0	0	0	1	0	0	1	1	47	63	36	59.06	208	46	57
101	1649897	SK	1	0	0	0	0	0	0	0	0	1	62	9	20	8.44	175	144	116
102	1727741	PK	1	0	0	0	0	0	0	0	1	4	41	34	15	31.88	152	72	75
103	1716907	KS	1	0	0	0	0	0	0	0	1	2	50	9	25	8.44	142	112	76

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The Principal
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Subject:: Approval of Plan of Thesis.

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Mudasir Bashir Sheikh**, a student of your college for **DM Medical Gastroenterology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Mucosal healing in ulcerative colits: a correlation study between white light endoscopy, linked color imaging and histology .

Supervisor	**Co-Supervisor:-**	**Co-Supervisor:-**
Dr. Varun Mehta	Dr. Ajit Sood	Dr. Sumit Grover
Professor	Prof. & Head,	Assoc. Professor
Dept. of Gastroenterology,	Dept. of Gastroenterology	Dept. of Pathology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

MUCOSAL HEALING IN ULCERATIVE COLITIS: A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DM

IN

GASTROENTEROLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES
FARIDKOT

NOVEMBER, 2022

DR. MUDASIR BASHIR SHEIKH

DEPARTMENT OF GASTROENTEROLOGY
DAYANAND MEDICAL COLLEGE &HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	MUCOSAL HEALING IN ULCERATIVE COLITIS : A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY
For the degree of	DM Gastroenterology
Name of the candidate	Dr. Mudasir Bashir Sheikh
Supervisor	Dr. Varun Mehta, Professor, Department of Gastroenterology, DMCH Ludhiana
Co-supervisor	Dr. Ajit Sood, Professor & Head, Department of Gastroenterology, DMCH Ludhiana Dr. Sumit Grover, Associate Professor, Department of Pathology, DMCH Ludhiana.
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Ulcerative colitis is a chronic inflammatory bowel disease of unknown etiology. Recently mucosal healing has emerged as an important therapeutic endpoint in ulcerative colitis. Mucosal healing is usually diagnosed and confirmed based on endoscopic observation using white light endoscopy. Recent studies recommend histological mucosal healing of intestinal tissue as a treatment target in ulcerative colitis. Linked color imaging is new endoscopic system that enhances the color differences of the gastrointestinal mucosa.

Aim of Study: To evaluate the endoscopic and histological disease activity in ulcerative colitis patients in symptomatic remission. To evaluate the correlation between white light endoscopy, linked colour imaging and histology in patients with ulcerative colitis in symptomatic remission.

Materials & Methods: All the patients enrolled in study from 1st January 2023 to 31st December 2023 will be evaluated by ELUXEO® 7000 endoscopic system (Fujifilm co., Tokyo, Japan). Target points will be seen using white light imaging (WLI) and linked color imaging (LCI) and mucosal biopsy will be taken for histological study from region of interest in each view. We will then evaluate the correlation between white light endoscopy, linked colour imaging and histological findings.

Clinical Significance: In the diagnosis of mucosal healing or histological activity in ulcerative colitis, multiple mucosal biopsies are performed, despite the invasiveness of the procedure, because it has been reported that endoscopic and histological activity sometimes differ in patients with inflammatory bowel disease. An endoscopic method is needed which can predict histological findings precisely with minimal invasion. Thus, if the mucosal inflammation of the patients with ulcerative colitis could be evaluated by endoscopic observation using linked-color imaging(LCI), without tissue biopsy, this would reduce the invasiveness of diagnostic examinations in patients with ulcerative colitis.

Keywords: Ulcerative colitis (UC), Linked color imaging (LCI).

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"MUCOSAL HEALING IN ULCERATIVE COLITIS: A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY"** exist in the Department of Gastroenterology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself under our supervision and guidance.

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3	COURSE OF STUDY AND SUBJECT	D.M. GASTROENTEROLOGY
4	DATE OF ADMISSION TO COURSE	29/04/2022
5	TITLE OF THE TOPIC	MUCOSAL HEALING IN ULCERATIVE COLITIS : A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY

6.0 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR STUDY

Ulcerative colitis is a chronic inflammatory bowel disease of unknown cause. Colonoscopy and biopsy have been used as the methods of choice to established diagnose the ulcerative colitis.[1] The incidence of ulcerative colitis is on rise in the western and Asian countries including India.[2-4] On average, 70-80% patients had a cumulative risk of relapse after 10years, and almost 50% of patients require ulcerative colitis related hospitalization, 10-year cumulative risk of colectomy is 10-15%.[5] Recently mucosal healing has emerged as an key therapeutic endpoint in ulcerative colitis. [6] Mucosal healing has been reported to reduce the rates of disease relapse, hospital admission and surgery, as well as lower the cumulative risk of dysplasia and colorectal cancer.[7-10] In recent clinical trials, endoscopic mucosal healing was defined as Mayo endoscopic score (MES) of 0 or 1 with conventional white-light imaging (WLI).[11] Mucosal healing is usually diagnosed and confirmed based on endoscopic observation using WLI.[12] It has been reported that histological intestinal inflammation is a major therapeutic target.[13-14]It has been seen that endoscopic and histological activity sometimes differ in patients with inflammatory bowel disease, so, multiple mucosal biopsies are performed to diagnosis the histological activity in ulcerative colitis, , despite the invasiveness of the procedure .[15] Hence an endoscopic method to predict the histological activity more accurately with minimal invasion is needed. Image-enhanced endoscopy (IEE) facilitates the detection and characterization of colorectal cancers.[16] Linked color imaging (LCI), a color enhancement function of the LASEREO System, has been developed as a new IEE technology, which makes red areas appear more redder and white areas appear more brighter. LCI is therefore useful tool for recognizing color differences in the mucosa, by facilitating the detection and recognition of colorectal neoplasms.[17-22] However there are few studies on the utility of linked-color imaging in the assessment of histological intestinal inflammation in ulcerative colitis

patients.[23,24] If the mucosal inflammation of the patients with ulcerative colitis could be evaluated by endoscopic observation using linked-color imaging, without tissue biopsy, this would reduce the invasiveness of diagnostic examinations in patients with ulcerative colitis. Therefore the aim of our study will be to evaluate the relationship between endoscopic mucosal healing, as assessed by white light imaging and linked color imaging, and histological activity in ulcerative colitis patients.

6.2 REVIEW OF LITERATURE-

Linked color imaging is useful tool for recognizing color differences in the mucosa, by facilitating the detection and recognition of colorectal neoplasms.[17-22] In the recent years there is data published showing the utility of linked-color imaging in the assessment of histological intestinal inflammation in ulcerative colitis patients. In a study authored by K. Uchiyama et al., published in Journal of Chron's and Colitis in 2017, investigated the efficacy of linked color imaging(LCI), a noval endoscopic enhancement system, for diagnosing mucosal inflammation in ilcerative colitis patients. Fifty two patients with ulcerative colitis were enrolled and 193 areas were assessed by LCI using LASEREO endoscopic system (Fujifilm Co., Tokyo, Japan). Region of interest (ROI) were set at biopsy sites, and red color in ROI was calculated from LCI index. Biopsy specimens were taken at each ROI and evaluated with Matts histopathological grade. Among areas with a Mayo endoscopic subscore of '0' 41.8% and 4.6% were classified as LCI-B, and LCI-C, respectively. Among areas with Mayo endoscopic subscore of '1' 60.5% and 34.6% were classified as LCI-C and LCI-B, respectively. The LCI index strongly correlated with the histopathological matts score.[23]

A pilot study conducted by Kanmura Shuji et al., on diagnostic utility of linked color imaging in the evaluation of colonic mucosal inflammation in ulcerative colitis. Twenty one patients of ulcerative colitis were evaluated by LASEREO system (Fujifilm Co., Tokyo, Japan). All of the target points were observed by conventional white light imaging(WLI) and LCI and biopsied from the ROI in each view. The color value of ROI was defined using international commission on illumination 1976 (L^*,$a^*$and b^*)/CIELAB. They then investigated the relationships among the color values, endoscopic findings and histological healing. The average LCI-a and LCI-b values of patients with high mucosal activity disease were significantly higher than in those with mucosal healing ($p<0.01$), and only LCI-a was

significantly correlated with the score for histological healing. It was concluded that the LCI is more useful than the WLI for visualization and evaluation of mucosal inflammation in ulcerative colitis.[24]

Takagi T. et al., did a study to investigate the efficacy of linked color imaging for the endoscopic diagnosis of mucosal healing in quiescent ulcerative colitis. Twenty six patients in ulcerative colitis remission, diagnosed with mayo endoscopic subscore '0'were enrolled. Using a LASEREO endoscopic system, endoscopic colonic images were assessed with LCI and colitis endoscopic index of severity. Endoscopic LCI images were separated into three subgroups (A- no redness, B- redness with visible vessels, C- redness without visible vessels). The Geboes score was used to evaluate histology, active mucosa was defined as GS>2B.1. Over a 48-month period, this study showed that LCI can be used to evaluate mucosal healing and predict long term outcomes in ulcerative colitis patients.[25]

In another study done by Kanmura S. et al., investigated the correlation between LCI observation and clinical relapse rate in ulcerative colitis patients. Fifty-eight patients who underwent colonoscopy were analysed. During 1-year follow up period, clinical relapse was observed in 12 patients (20.1%) among which ten patients (83.3%) had an LCI-scarlet color lesions recognized by LCI. By contrast, 29 patients (63%) had no LCI- scarlet color lesions in the clinical remission group (n=46). There was a significant difference in the LCI-scarlet color between the clinical relapse and remission groups, remaining significantly associated with clinical relapse. LCI findings, including an orange-like color lesion, have diagnostic implications for predicting the risk of clinical relapse in ulcerative colitis during the 1-year follow-up period.[26]

The efficacy of linked color imaging for the endoscopic diagnosis of mucosal healing in quiescent ulcerative colitis was studied by Tomohisa T. et al. The study included 26 patients with ulcerative colitis in remission,

endoscopic colonic images were assessed with linked color imaging and the colitis endoscopic index of severity. The LCI-A group did not relapse, and the non-relapse rate was significantly higher (P=0.018) than that in LCI-B group. It was concluded that this methodology can be used to evaluate mucosal healing and predict long-term outcomes in ulcerative colitis patients.[27]

6.3 AIMS AND OBJECTIVES-

- To evaluate the endoscopic and histological disease activity in ulcerative colitis patients in symptomatic remission.
- To evaluate the correlation between white light endoscopy, linked colour imaging and histology in patients with ulcerative colitis in symptomatic remission.

7.0 MATERIAL AND METHODS:

7.1 SOURCE OF DATA:

All the patients with ulcerative colitis in symptomatic remission attending gastroenterology out-patient department at Dayanand Medical College and Hospital, Ludhiana, Punjab, India between January 1, 2023 and December 31, 2023.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA-

Adults (>18 years of age) with established ulcerative colitis in symptomatic remission will be enrolled.

Symptomatic remission will be defined as normal stool frequency and no bleeding per rectum, and normal physician global assessment as depicted by partial Mayo clinic score of 0-1.[28]

Exclusion Criteria

Patients with ulcerative colitis with disease activity (defined as partial Mayo clinic score >1), infectious colitis, severe co-morbid cardiovascular, pulmonary, renal or neurological illness, pregnancy and lactation will be excluded.

Study Protocol

Written informed consent will be taken from all the patients. Demographic details will be obtained. Background information about ulcerative colitis will be noted including duration of disease, extent of ulcerative colitis, clinical course, and treatment taken including biologics therapy.

All patients will be given routine bowel preparation with 2 litres polyethylene glycol 3350, sodium chloride, sodium hydrogen carbonate and potassium chloride concentrate for oral solution.

A high definition EC-760ZP-V/L endoscope will be used as part of the ELUXEO® 7000 endoscopic system that consists of VP-7000 processor and BL-7000 light source (Fujifilm Medical Co., Tokyo, Japan) in all colonoscopy/sigmoidoscopic examinations. This endoscopic system is capable of producing light suitable for white light imaging and linked colour imaging. Colonoscopy/sigmoidoscopic examination will be performed by one experienced endoscopist. The endoscopic images with WLI and LCI will be captured from the same position in a row before biopsy, then the biopsy will be performed targeting the reddest site in the observed area while capturing the images during the biopsy for reference of the biopsied point. In each case MES[29] and UCEIS[30] will be evaluated under WLI observation. Endoscopic LCI images will be separated into three subgroups (A-no redness, B-redness with visible vessels, C- redness without visible vessels)

The endoscopic images obtained by WLI and LCI before the biopsy will be analysed.

The histological examination of all the biopsy specimens will be performed by an experienced pathologist who will be blinded to the patient's endoscopic activity. The histological assessment will be based on Nancy index.[31]

DURATION OF THE STUDY-

One year from 1st January 2023 till 31st December 2023.

OUTCOME

Correlation between white light endoscopy, linked colour imaging and histological activity in patients with ulcerative colitis in symptomatic remission.

STATISTICAL ANALYSIS

The results will be analysed using Mann-Whitney U test, or Wilcoxon signed-rank test, as appropriate. Correlation coefficients will be calculated by a Spearman's rank correlation analysis. The discriminatory power of each putative marker will be described using the receiver operating characteristics area under curve (ROC-AUC). All statistical analysis will be conducted using SPSS software program (version 21, SPSS Inc., Chicago, Illinois, USA). P values < 0.05 will be considered statistical significant.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes, Routine lab investigation and colonoscopy/sigmoidoscopy.

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes, attached herewith

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PROFORMA

Name			
Age		Sex	
MRD		Contact number	
Address			

Co-morbidities (Yes/No)	Hypertension		Diabetes	
	Bronchial asthma		COAD	
	Coronary artery disease		Cerebrovascular disease	
	Thyroid disorders		Arthritis	
	Migraine/ Headache		Others	

Addictions	Type	Quantity	Remarks
Smoking	Bidi Cigarette		
Alcohol	Beer Wine Whisky Gin Vodka Rum Country liquor		
Opium	Poppy flower (Afeem) Poppy husk (Bhukki) Poppy straw (Doda)		
Intravenous drug users			
Others			

Age of onset of symptoms (in years)		
Age at diagnosis (in years)		
Year of diagnosis		
Disease Duration (in years)		
Disease Extent	Extensive Colitis (E_3)	
	Left sided (E_2)	
	Proctitis (E_1)	
Family History of IBD	Yes	No

Partial Mayo Score	SCCAI (Simple clinical colitis activity index)
Stool frequency	Bowel frequency (Per day)

Signature of Candidate **Signature of Super visor i**

0 = Normal 1 = 1-2 stools/day more than normal 2 = 3-4 stools/day more than normal 3 = >4 stools/day more than normal Rectal bleeding 0 = None 1 = Visible blood with stool less than half the time 2 = Vissible blood with stool half of the time or more 3 = Passing blood alone Physician rating of disease activity 0 = Normal 1 = Mild 2 = Moderate 3 = Severe	1-3 = 0 4-6 = 1 7-9 = 2 >9 = 3 Bowel frequency (Per night) 0 = 0 1-3 = 1 4-6 = 2 Urgency of defecation None = 0 Hurry = 1 Immediately = 2 Incontinence = 3 Blood in stool None = 0 Trace = 1 Occasionally frank = 2 Usually frank = 3 General well being Very well = 0 Slightly below par = 1 Poor = 2 Very poor = 3 Terrible = 4 Extra-colonic manifestations Uveitis, pyoderma gangrenosum, erythema nodosum, arthropathy = 1 per manfestation
Total score =	Total score =

IBD-DISK (For each of the ten statements below, score your level of agreement on a scale of 0 to 10)		Score 0- Absolutely disagree 10- Absolutely agree
Abdominal pain	I have had aches or pains in my stomach or abdomen	
Regulating defecation	I have had difficulty coordinating and managing defecation, including choosing and getting to an appropriate place for defecation and cleaning myself afterwords	

Signature of Candidate **Signature of Super visor ii**

Interpersonal interactions	I have had difficulty with personal relationships and /or difficulty participating in the community	
Education and work	I have had difficulty with school or studying activities, and /or difficulty with work or household activities	
Sleep	I have had difficulty sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning	
Energy	I have not felt rested and refreshed during the day, and have felt tired and without energy	
Emotions	I have felt sad, low or depressed, and/or worried or anxious	
Body image	I have not liked the way my body or body parts look	
Sexual functions	I have had difficulty with the mental and/or physical aspects of sex	
Joint pains	I have had pains in the joints of my body	

Height (in cm)	
Weight (in kg)	
BMI (kg/m^2)	
Mid-arm circumference (in cm)	
Hand grip strength	

Hemoglobin (gm/dl)	
PCV (%)	
MCV (fl)	
Platelets (10^3/ul)	
ESR (mm1st-hour)	
CRP (mg/lt)	
Fecal calprotectin (ug/gm)	
Albumin (gm/dl)	
TLC (10^3/ul)	

Last Colonoscopy/Sigmoidoscopy	
Date	
Disease extent	Extensive Colitis (E_3) Left sided (E_2) Proctitis (E_1)
Mayo endoscopic score (MES)	
UCEIS	

Signature of Candidate **Signature of Super visor iii**

Treatment

Previous Treatment	5-ASA Thiopurines Tofacitinib Anti-TNFs Anti Integrins FMT Others		
Current Treatment	5-ASA Thiopurines Tofacitinib Anti-TNFs Anti Integrins FMT Others		

Endoscopic Findings

White Light Imaging (WLI)	Linked Color Imaging (LCI)
Mayo endoscopic score Normal=0 Mild disease - Erythema, decreased vascular pattern, mild friability = 1 Moderate - Marked erythema, absent vascular pattern, friability, erosions = 2 Severe - Spontaneous bleeding, ulceration = 3 **UCIES** **Vascular pattern** Normal=0 Patchy Oblitrated=1 Oblitrated=2 **Bleeding** None=0 Mucosal=1 Luminal mild=2 Luminal moderate/severe=3 **Esosion and ulcers** None=0 Erosions=1 Superficial ulcers=2 Deep ulcers=3	A = No redness B = Redness with visible vessels C = Redness without visible vessels

Signature of Candidate **Signature of Super visor v**

Histological findings

Nancy histological index	Geboes histological score	Robarts histopathology index
Grade 0 = No histological significant disease Grade 1 = Chronic inflammatory infiltrate with no acute inflammatory infiltrate Grade 2 = Mild active disease Grade 3 = Moderately active disease Grade 4 = Severely active disease	Gebos Histological score **Grade 0** = Structural (architectural changes) 0: No abnormality 0.1 : Mild abnormality 0.2 : Mild or moderate diffuse or multifocal abnormalities 0.3 : Severe diffuse or multifocal abnormalities **Grade 1** = Chronic inflammatory infiltrate 1 : No increase 1.1 : Mild but unequivocal increase 1.2 Moderate increase 1.3 Marked increase **Grade 2** = Lamina propria neutrophils and eosinophils 2A : Eosinophils 2A.0 : No increase 2A.1 : Mild but unequivocal increase 2A.2 : Moderate increase 2A.3 : Marked increase 2B : Neutrophils 2B.0 : None 2B.1 : Mild but unequivocal increase 2B.2 : Moderate increase 2B.3 : Marked increase **Grade 3** = Neutrophils in epithelium 3.0 None 3.1 : < 5% crypt involved 3.2 : < 50% crypt involved 3.3 : > 50% crypt involved **Grade 4** = Crypt destruction	Chronic inflammatory infiltrate 0 = No increase 1 = mild but unequivocal increase 2 = Moderate increase 3 = Marked increase Lamina propria neutrophils 0 = No increase 1 = mild but unequivocal increase 2 = Moderate increase 3 = Marked increase Neutrophils in epithelium 0 None 1 = < 5% crypt involved 2 = < 50% crypt involved 3 = > 50% crypt involved Erosion or ulceration 0= No erosion, ulceration, or granulation tissue 1 = Recovering epithelium plus adjacent inflammation 1 = Probable erosion – focally stripped 2 = Unequivocal erosion 3 = Ulcer or granulation tissue Calculating the Robart's histopathology index : RHI = 1 X chronic inflammatory cell infiltrate level [4 levels] + 2 X Lamina propria neutrophils [4 levels] + 3 X epithelial neutrophils [4 levels] + 5 X erosion or ulceration [4 levels]

	4.0 : None 4.1 : Probable- local excess of neutrophils in part of crypt 4.2 : Probable- Marked attenuation 4.3 : Unequivocal crypt destruction **Grade 5** = Erosion or ulceration 5.0 : No erosion, ulceration, or granulation tissue 5.1 : Recovering epithelium plus adjacent inflammation 5.2 : Probable erosion – focally stripped 5.3 : Unequivocal erosion 5.4 : Ulcer or granulation tissue	

INFORMED PATIENT CONSENT

Date: _____

I……..D/o, W/o, S/o…… ……am willing to participate in the study **"MUCOSAL HEALING IN ULCERATIVE COLITIS : A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"MUCOSAL HEALING IN ULCERATIVE COLITIS : A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

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गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक केहस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“MUCOSAL HEALING IN ULCERATIVE COLITIS : A CORRELATION STUDY BETWEEN WHITE LIGHT ENDOSCOPY, LINKED COLOR IMAGING AND HISTOLOGY” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ। ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕ ਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ